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     FILE 'MEDLINE' ENTERED AT 08:29:24 ON 26 AUG 1997
                E BELL G/AU
L1           488 S E3,E11
L2            10 S L1 AND OPI?
L3         10807 S RECEPTORS, OPIOID + NT/CT
L4          7522 S L3/MAJ
L5         13746 S LIGANDS/CT
L6           715 S L5/MAJ
L7            17 S L4 AND L6
L8           431 S L3 AND L5
L9           312 S L8 AND PY<1995
L10           86 S L9 AND (LIGAND? AND OPI?)/TI
L11           76 S L10 NOT L7
L12           47 SORT L11 TAG PY D
L13           38 S L3 AND CHIM?
L14           12 S L5 AND L13
L15            7 S L3 AND (CHIM?(2A)OPIOID RECEP?)

     FILE 'MEDLINE' ENTERED AT 09:13:57 ON 26 AUG 1997
L16           47 S L12
L17           70 S L7 OR L12 OR L15

     FILE 'MEDLINE' ENTERED AT 09:14:56 ON 26 AUG 1997

=> d l17 1-70 bib ab ct

L17  ANSWER 1 OF 70  MEDLINE
AN   97229262     MEDLINE
TI   Neuroprotective and anti-amnesic potentials of sigma (sigma)
     receptor ligands.
AU   Maurice T; Lockhart B P
CS   INSERM U. 336, Developpement, Plasticite et Vieillissement du
     Syst`eme Nerveux, ENSCM, Montpellier, France.. maurice@cit.enscm.fr
SO   PROGRESS IN NEURO-PSYCHOPHARMACOLOGY AND BIOLOGICAL PSYCHIATRY,
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(1997 Jan) 21 (1) 69-102. Ref: 224
Journal code: Q45. ISSN: 0278-5846.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 9709
EW 19970901

AB 1. Although the physical nature of sigma (sigma) receptors have not yet been fully defined, several classes of selective ligands have been characterised, demonstrating a plethora of physiological actions. In the present review, the authors have set out to highlight two important aspects of the biological activities of sigma ligands, their neuroprotective and anti-amnesic effects. 2. The sigma ligands present a therapeutic potential as neuroprotective agents in brain ischemia. The neuroprotective activity of many non-selective sigma ligands is primarily a result of their affinity for the NMDA receptor complex. However, selective sigma ligands are also neuroprotective, possibly by inhibition of the ischemic-induced presynaptic release of excitotoxic amino acids. 3. The sigma 1 ligands prevent the experimental amnesia induced by muscarinic cholinergic antagonists at either the learning, consolidation or retention phase of the mnesic process. This effect involves a potentation of acetylcholine release induced by sigma 1 ligands selectively in the hippocampal formation and cortex. 4. The sigma 1 receptor ligands also attenuate the learning impairment induced by dizocilpine, a non-competitive antagonist of the NMDA receptor, and may relate to the potentiating effect of sigma 1 ligands on several NMDA receptor-mediated responses previously described in vitro and in vivo in the hippocampus. This effect is shared by NPY- and CGRP-related peptides and by neuroactive steroids, confirming the in vitro evidences of functional interactions between the sigma 1 receptors and these different systems. 5. Additional amnesia models also seem to be alleviated by sigma 1 ligands, such as phencyclidine-induced cognitive dysfunctions, and amnesia induced by the calcium channel blocker nimodipine, or by exposure to carbon monoxide. Furthermore, a preliminary study in an animal model of age-related memory deficits, the senescence-accelerated mouse, strengthened the therapeutic potentials of selective sigma 1 receptor ligands in aging-related pathologies.

CT Check Tags: Animal
*Amnesia: DT, drug therapy
***Ligands**
Mice
*Neuroprotective Agents: PD, pharmacology
***Receptors, sigma: DE, drug effects**

L17 ANSWER 2 OF 70 MEDLINE

AN 96303004 MEDLINE
TI delta-Opioid receptor: the third extracellular loop determines naltrindole selectivity.
AU Li X; Varga E V; Stropova D; Zalewska T; Malatynska E; Knapp R J; Roeske W R; Yamamura H I
CS Department of Pharmacology, College of Medicine, University of Arizona, Tucson 85724, USA.
SO EUROPEAN JOURNAL OF PHARMACOLOGY, (1996 Apr 4) 300 (1-2) R1-2.
Journal code: EN6. ISSN: 0014-2999.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9612
AB Human delta/mu-**opioid receptor chimeras** were constructed to determine the role of the second and third extracellular loops in alkaloid ligand selectivity. Exchanging the third extracellular loop of the delta-opioid receptor with that of the mu-opioid receptor dramatically decreased the affinity of naltrindole, but not that of morphine. The results suggest that different domains of the opioid receptor are involved in the binding of naltrindole and morphine.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Base Sequence
Binding Sites
Cercopithecus aethiops
Chimera
Molecular Sequence Data
*Naltrexone: AA, analogs & derivatives
Naltrexone: ME, metabolism
*Narcotic Antagonists: ME, metabolism
Polymerase Chain Reaction
Receptors, Opioid, delta: CH, chemistry
***Receptors, Opioid, delta: ME, metabolism**
Sequence Alignment

L17 ANSWER 3 OF 70 MEDLINE
AN 96109281 MEDLINE
TI Studies on mu and delta **opioid receptor** selectivity utilizing **chimeric** and site-mutagenized receptors.
AU Wang W W; Shahrestanifar M; Jin J; Howells R D
CS Department of Biochemistry and Molecular Biology, New Jersey Medical School, Newark 07103, USA.
NC 2 S07 RR05393 (NCRR)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1995 Dec 19) 92 (26) 12436-40.
Journal code: PV3. ISSN: 0027-8424.
CY United States

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9608
AB Opioid receptors are members of the guanine nucleotide binding protein (G protein)-coupled receptor family. Three types of opioid receptors have been cloned and characterized and are referred to as the delta, kappa and mu types. Analysis of receptor chimeras and site-directed mutant receptors has provided a great deal of information about functionally important amino acid side chains that constitute the ligand-binding domains and G-protein-coupling domains of G-protein-coupled receptors. We have constructed delta/mu **opioid receptor chimeras** that were express in human embryonic kidney 293 cells in order to define receptor domains that are responsible for receptor type selectivity. All chimeric receptors and wild-type delta and mu opioid receptors displayed high-affinity binding of etorphine (an agonist), naloxone (an antagonist), and bremazocine (a mixed agonist/antagonist). In contrast, chimeras that lacked the putative first extracellular loop of the mu receptor did not bind the mu-selective peptide [D-Ala2,MePhe4,Gly5-ol]enkephalin (DAMGO). Chimeras that lacked the putative third extracellular loop of the delta receptor did not bind the delta-selective peptide, [D-Ser2,D-Leu5]enkephalin-Thr (DSLET). Point mutations in the putative third extracellular loop of the wild-type delta receptor that converted vicinal arginine residues to glutamine abolished DSLET binding while not affecting bremazocine, etorphine, and naltrindole binding. We conclude that amino acids in the putative first extracellular loop of the mu receptor are critical for high-affinity DAMGO binding and that arginine residues in the putative third extracellular loop of the delta receptor are important for high-affinity DSLET binding.
CT Check Tags: Comparative Study; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Analgesics: ME, metabolism
Base Sequence
Benzomorphans: ME, metabolism
Binding, Competitive
Cell Line
Cell Membrane: PH, physiology
Cell Membrane: UL, ultrastructure
Chimeric Proteins: AI, antagonists & inhibitors
Chimeric Proteins: BI, biosynthesis
*Chimeric Proteins: ME, metabolism
Enkephalin, Leucine: AA, analogs & derivatives
Enkephalin, Leucine: ME, metabolism
Enkephalins: ME, metabolism
Etorphine: ME, metabolism
G-Proteins: ME, metabolism
Kidney

Kinetics
Molecular Sequence Data
Mutagenesis, Site-Directed
Naloxone: ME, metabolism
Oligodeoxyribonucleotides
Polymerase Chain Reaction
*Protein Structure, Secondary
Receptors, Opioid, delta: AI, antagonists & inhibitors
Receptors, Opioid, delta: BI, biosynthesis
***Receptors, Opioid, delta: ME, metabolism**
Receptors, Opioid, mu: AI, antagonists & inhibitors
Receptors, Opioid, mu: BI, biosynthesis
***Receptors, Opioid, mu: ME, metabolism**
Substrate Specificity
Transfection

L17 ANSWER 4 OF 70 MEDLINE
AN 96083806 MEDLINE
TI (E)-8-benzylidene derivatives of 2-methyl-5-(3-hydroxyphenyl)morphans: highly selective ligands for the sigma 2 receptor subtype.
AU Bertha C M; Vilner B J; Mattson M V; Bowen W D; Becketts K; Xu H; Rothman R B; Flippen-Anderson J L; Rice K C
CS Laboratory of Medicinal Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland 20892, USA.
SO JOURNAL OF MEDICINAL CHEMISTRY, (1995 Nov 24) 38 (24) 4776-85. Journal code: J0F. ISSN: 0022-2623.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9603
AB The determination of the structure and function of the sigma receptor subtypes and their physiological role(s) has been impeded by the unavailability of selective ligands. We have developed a new class of sigma subtype selective receptor ligands that are (E)-8-benzylidene derivatives of the synthetic opioid (+/-)-, (+)-, and (-)-2-methyl-5-(3-hydroxyphenyl)morphan-7-one (1). The derivatives can be prepared by reaction of 1, (+)-1, and (-)-1 with the appropriate benzaldehyde under Claisen-Schmidt conditions. Incorporation of substituted (E)-8-benzylidene moieties onto the 7-keto precursor of (+)-2-methyl-5-(3-hydroxyphenyl)morphan, (+)-1, produces compounds (-)-2 through (-)-7 (5.8-32.0 nM, sigma 1), which have between a 25- and 131-fold increase in affinity for the sigma 1 receptor subtype relative to the keto precursor (+)-1 (Ki = 762 nM, sigma 1). Compound (-)-2 is the most selective of this group (16-fold) for the sigma 1 subtype versus sigma 2. Substitution of an (E)-8-benzylidene moiety onto the 7-keto precursor of (-)-2-methyl-5-(3-hydroxyphenyl)morphan, (-)-1, produces compounds

(+)-2-(+)-9 (6.4-52.6 nM, sigma 2), which have at least a 475-3906-fold increase in affinity for the sigma 2 receptor subtype relative to the keto precursor (-)-1 (Ki = 25 x 10(3) nM). This enhancement of sigma 2 receptor affinity is accompanied by substantial selectivity of all of these dextrorotatory products for the sigma 2 relative to the sigma 1 subtype (32-238-fold), and thus, they are among the most sigma 2 selective compounds currently known. Furthermore, the sigma 1 subtype is highly enantioselective for the levorotatory isomers, (-)-2-(-)-7 (41-1034-fold), whereas the sigma 2 subtype is only somewhat enantioselective for the dextrorotatory isomers, (+)-2-(+)-7 (2.6-9.3-fold). All of these derivatives retain substantial affinity for the mu opioid receptor. Despite the high affinity of the dextrorotatory derivatives for the mu opioid receptor, the high affinity and selectivity for sigma 2 over sigma 1 sites will surely prove beneficial as tools for the delineation of the function and physiological role of sigma 2 receptors.

CT Check Tags: Animal; Male; Support, U.S. Gov't, P.H.S.
*Benzylidene Compounds: CH, chemistry
Benzylidene Compounds: CS, chemical synthesis
*Benzylidene Compounds: PD, pharmacology
Binding Sites
Brain: DE, drug effects
Brain: ME, metabolism
Guinea Pigs
***Ligands**
Radioligand Assay
Rats
Rats, Sprague-Dawley
***Receptors, sigma: DE, drug effects**
Receptors, sigma: ME, metabolism
Stereoisomerism
Structure-Activity Relationship

L17 ANSWER 5 OF 70 MEDLINE
AN 95327063 MEDLINE
TI Analysis of selective binding epitopes for the kappa-opioid receptor antagonist nor-binaltorphimine.
AU Hjorth S A; Thirstrup K; Grandy D K; Schwartz T W
CS Department of Clinical Biochemistry, Rigshospitalet, Copenhagen, Denmark..
NC DA08562 (NIDA)
SO MOLECULAR PHARMACOLOGY, (1995 Jun) 47 (6) 1089-94.
Journal code: NGR. ISSN: 0026-895X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9510
AB The structural determinants for the selective binding of the nonpeptide opioid receptor antagonist nor-binaltorphimine (nor-BNI)

to the kappa-opioid receptor were characterized using a systematic series of chimeras between the kappa receptor and the homologous mu-**opioid receptor**. All 10 **chimeric**
constructs bound the nonselective antagonists (-)-naloxone and diprenorphine with similar affinities, as did the two wild-type receptors. Introduction of amino-terminal segments of increasing length, extending to and including transmembrane segment VI, from the mu receptor into the kappa receptor did not impair the high affinity binding of nor-BNI, and neither did introduction of the intracellular carboxyl-terminal extension of the mu receptor. In contrast, nor-BNI binding was impaired > or = 600-fold in constructs in which extracellular loop 3 and transmembrane segment VII originated from the mu receptor. The exchange of a single residue within this region, Glu297, for lysine, the corresponding residue from the mu receptor, reduced the binding affinity of nor-BNI 142-fold, without affecting the binding the nonselective compounds (-)-naloxone and diprenorphine. It is concluded that the selective binding of nor-BNI to the kappa-opioid receptor is determined by nonconserved residues located in extracellular loop 3 and transmembrane segment VII and that Glu297, located just outside transmembrane segment VI, plays a major role in the kappa-selective binding characteristics of nor-BNI.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
*Epitopes: AN, analysis
Glutamine: GE, genetics
Molecular Sequence Data
*Naltrexone: AA, analogs & derivatives
Naltrexone: ME, metabolism
Naltrexone: PD, pharmacology
Rats
***Receptors, Opioid, kappa: AI, antagonists & inhibitors**
Receptors, Opioid, kappa: GE, genetics
Receptors, Opioid, kappa: IM, immunology
Receptors, Opioid, kappa: ME, metabolism
Receptors, Opioid, mu: GE, genetics
Recombinant Fusion Proteins

L17 ANSWER 6 OF 70 MEDLINE
AN 95286574 MEDLINE
TI The third extracellular loop of the mu opioid receptor is important for agonist selectivity.
AU Xue J C; Chen C; Zhu J; Kunapuli S P; de Riel J K; Yu L; Liu-Chen L Y
CS Department of Pharmacology, Temple University School of Medicine, Philadelphia, Pennsylvania 19140, USA..
NC DA 04745 (NIDA)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Jun 2) 270 (22) 12977-9.
Journal code: HIV. ISSN: 0021-9258.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9509
AB To investigate the interaction between the mu opioid receptor and its ligands, we compared the binding of mu-selective ligands to two mu/kappa **chimeric opioid receptors** and to mu and kappa receptors. The two chimeras were constructed from cloned rat mu and kappa receptors in which a segment from the middle of the third intracellular loop to the C terminus was exchanged. When this portion of the kappa receptor was replaced by that of the mu receptor, affinities of mu selective agonists, DAMGO (Tyr-D-Ala-Gly-NMePhe-Gly-ol), PL017 (Tyr-Pro-NMePhe-D-Pro-NH2), sufentanil, and morphine, were greatly increased as compared to those for the kappa receptor. Conversely, when this region of the mu receptor was substituted by that of the kappa receptor, affinities for these agonists were substantially decreased as compared with those of the mu receptor. Unlike selective agonists, the mu-selective antagonist, CTAP (D-Phe-Cys-Tyr-D-Trp-Arg-Thr-penicillamine-Thr-NH2), displayed a low affinity for both chimeric receptors, similar to that of the kappa receptor. Thus, the region from the middle of the third intracellular loop to the C terminus of the mu receptor is important for the binding of selective agonists. Conversely, the determinants for selective binding of the antagonist CTAP reside in a more extended region of the receptor.
CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Binding Sites
Cell Line
Diprenorphine: ME, metabolism
Endorphins: ME, metabolism
Endorphins: PD, pharmacology
Enkephalins: ME, metabolism
Enkephalins: PD, pharmacology
Molecular Sequence Data
Morphine: ME, metabolism
Morphine: PD, pharmacology
Protein Conformation
Rats
Receptors, Opioid, mu: AG, agonists
***Receptors, Opioid, mu: CH, chemistry**
Receptors, Opioid, mu: ME, metabolism
Sufentanil: ME, metabolism
Sufentanil: PD, pharmacology

L17 ANSWER 7 OF 70 MEDLINE
AN 95255606 MEDLINE
TI Molecular biology and pharmacology of cloned opioid receptors.

AU Knapp R J; Malatynska E; Collins N; Fang L; Wang J Y; Hruby V J; Roeske W R; Yamamura H I

CS Department of Pharmacology, University of Arizona, Tucson 85724, USA..

NC DA-04248 (NIDA)
DA-06284 (NIDA)
DA-08657 (NIDA)

SO FASEB JOURNAL, (1995 Apr) 9 (7) 516-25. Ref: 65
Journal code: FAS. ISSN: 0892-6638.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LA English

FS Priority Journals; Cancer Journals

OS GENBANK-U07882; GENBANK-L25119; GENBANK-U11053

EM 9508

AB The cloning and expression of DNA for the three major opioid receptor types (mu, delta, and kappa) present new research opportunities for the characterization of opioid drugs and their interactions with these receptors. Genomic and cDNA clones for opioid receptors exist for several animal species including mouse, rat, guinea pig, and human. These include clones for all three human opioid receptor types. The receptor proteins consist of about 400 amino acids and have the characteristic seven transmembrane domain structure of G-protein-coupled receptors. There is about 60% amino acid identity between opioid receptor types and about 90% identity between a receptor type cloned from different animal species. All opioid receptor types mediate the inhibition of adenylyl cyclase in response to agonist binding. Radioligand binding and functional studies using the cloned receptors tend to support current conclusions on opioid drug receptor selectivity and activity. Investigations of **opioid receptor chimeras** and single amino acid mutants are providing information on the ligand recognition sites of these receptors and essential support for the development of computational opioid receptor models. A molecular model of the human delta opioid receptor is included in this review.

CT Check Tags: Animal; Human; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Cloning, Molecular
Ligands
Models, Molecular
Molecular Sequence Data
Receptors, Opioid: DE, drug effects
***Receptors, Opioid: GE, genetics**
***Receptors, Opioid: ME, metabolism**
Recombinant Proteins: DE, drug effects
Recombinant Proteins: ME, metabolism

L17 ANSWER 8 OF 70 MEDLINE
AN 95100592 MEDLINE
TI [Analgesic properties of different ligands of opioid receptors]. Analgeticheskie svoistva razlichnykh ligandov opioidnykh retseptorov.
AU Chichenkov O N
SO ANESTEZIOLOGIIA I REANIMATOLOGIIA, (1994 Jul-Aug) (4) 5-8. Journal code: 4ST. ISSN: 0201-7563.
CY RUSSIA: Russian Federation
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
EM 9503
CT Check Tags: Comparative Study; Human
*Analgesics, Opioid
Analgesics, Opioid: ME, metabolism
***Ligands**
***Receptors, Opioid**
Receptors, Opioid: ME, metabolism
Receptors, Opioid, delta: ME, metabolism
Receptors, Opioid, mu: ME, metabolism

L17 ANSWER 9 OF 70 MEDLINE
AN 95074012 MEDLINE
TI Differential binding domains of peptide and non-peptide **ligands** in the cloned rat kappa **opioid** receptor.
AU Xue J C; Chen C; Zhu J; Kunapuli S; DeRiel J K; Yu L; Liu-Chen L Y
CS Department of Pharmacology, Temple University School of Medicine, Philadelphia, Pennsylvania 19140.
NC DA 04745 (NIDA)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, **(1994 Dec 2)** 269 (48) 30195-9. Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9503
AB This study was to identify specific regions in kappa opioid receptors that accounted for binding selectivity of kappa ligands. Six chimeric mu/kappa receptors were constructed from cloned rat kappa and mu opioid receptors and transiently expressed in COS-1 cells. All six chimeric mu/kappa receptors bound [3H] diprenorphine with high affinities, indicating that these **chimeras** retain **opioid receptor** conformation. Binding affinities of three peptide ligands (dynorphin A, alpha-neo-endorphin, and dynorphin B) and three nonpeptide ligands (norbinaltorphimine, U50,488H, and U69,593) for chimeras were determined and compared to those for mu and kappa opioid receptors. The second extracellular loop and the adjoining C-terminal portion of the fourth transmembrane helix were essential for the high

affinity binding of dynorphin A, alpha-neo-endorphin, and dynorphin B to the kappa receptor. The third extracellular loop and the sixth and seventh transmembrane helices played an important role in determining the selectivity of nor-binaltorphimine for the kappa over the mu receptor. U50,488H and U69,593 appeared to require the whole kappa receptor except the second extracellular loop to attain high affinity binding. Thus, the kappa opioid receptor has differential binding domains for peptide and non-peptide ligands.

CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Base Sequence
Binding Sites
Binding, Competitive
Cell Line
Cercopithecus aethiops
Chimeric Proteins: BI, biosynthesis
Chimeric Proteins: CH, chemistry
Chimeric Proteins: ME, metabolism
Cloning, Molecular
Diprenorphine: ME, metabolism
Dynorphins: ME, metabolism
DNA Primers
*Endorphins: ME, metabolism
Kinetics
Ligands
Molecular Sequence Data
Naltrexone: AA, analogs & derivatives
Naltrexone: ME, metabolism
Polymerase Chain Reaction
Protein Conformation
Protein Structure, Secondary
Pyrrolidines: ME, metabolism
Rats
Receptors, Opioid: AG, agonists
Receptors, Opioid, kappa: BI, biosynthesis
Receptors, Opioid, kappa: CH, chemistry
***Receptors, Opioid, kappa: ME, metabolism**
Receptors, Opioid, mu: ME, metabolism
Transfection

L17 ANSWER 10 OF 70 MEDLINE
AN 95049076 MEDLINE
TI Delta **opioid** receptor selective **ligands**; DPLPE-deltorphin chimeric peptide analogues [published erratum appears in Int J Pept Protein Res 1994 Dec;44(6):607].
AU Misicka A; Lipkowski A W; Horvath R; Davis P; Porreca F; Yamamura H I; Hruby V J
CS Department of Chemistry, University of Arizona, Tucson..
NC DA 06284 (NIDA)
NS-19972 (NINDS)

SO INTERNATIONAL JOURNAL OF PEPTIDE AND PROTEIN RESEARCH, **(1994 Jul)** 44 (1) 80-4.
Journal code: GSD. ISSN: 0367-8377.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9502
AB Further efforts to correlate the topography of the bioactive structures of DPDPE and the deltorphins, two delta-opioid receptor active peptide families, are reported. A number of DPLPE-deltorphin chimeric peptides have been synthesized in which the C-terminal dipeptide delta-address of the deltorphins (-Val-GlyNH2, -Nle-GlyNH2) have been linked to the highly delta-opioid selective cyclic peptides DPDPE or DPLPE. These studies demonstrate that a major structural feature determining high potency of hybrid analogues is the chirality of the amino acid residue in position 5. The radioligand binding assays have revealed a decrease in potency (compared to DPDPE) at delta-receptors when the C-terminal dipeptides were added to DPDPE. On the other hand, chimeric peptides of DPLPE with these same C-terminal dipeptides retained high delta-selectivity and affinity. Similar results were obtained using the mouse vas deferens (MVD) and guinea pig ileum (GPI) bioassays. The importance of the hydrophilicity of amino acids in positions 2 and 5 for delta-selectivity is consistent with the previous finding for DPLPE and DPDPE. On the other hand, the replacement of phenylalanine-4 with p-chlorophenylalanine-4 did not increase delta-selectivity as in DPDPE. These findings suggest that the delta-receptor interacts with hybridized enkephalins and deltorphins somewhat differently than with DPDPE.
CT Check Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
*Enkephalins: CS, chemical synthesis
Ligands
Molecular Sequence Data
*Oligopeptides: CS, chemical synthesis
Radioligand Assay
***Receptors, Opioid, delta: AG, agonists**

L17 ANSWER 11 OF 70 MEDLINE
AN 94349130 MEDLINE
TI Behavioral evidence for a modulating role of sigma ligands in memory processes. II. Reversion of carbon monoxide-induced amnesia.
AU Maurice T; Hiramatsu M; Kameyama T; Hasegawa T; Nabeshima T
CS Department of Neuropsychopharmacology and Hospital Pharmacy, Nagoya University School of Medicine, Japan..
SO BRAIN RESEARCH, (1994 May 30) 647 (1) 57-64.
Journal code: B5L. ISSN: 0006-8993.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals
EM 9412
AB This study examined the effect of low doses of sigma ligands on amnesia induced in mice by successive carbon monoxide (CO) exposure. Mice were exposed three consecutive times to CO (10 ml/min, 30-50 s) at 38 degrees C. Spatial working memory impairment was investigated 5 days later by monitoring spontaneous alternation behavior in a Y-maze. Delayed amnesia was examined 7 days after CO exposure by using a step-down passive avoidance test. The preadministration of the sigma ligand 1,3-di-(2-tolyl)guanidine (DTG), at doses of 1 to 1000 microgram/kg, s.c., 30 min before CO exposure did not affect the resulting amnesia in either test. However, when administered 30 min before the test, i.e., 5 or 7 days after CO exposure, this agent completely reversed the CO-induced decrease in alternation performance, at doses of 10 to 100 micrograms/kg. The same effect was observed with (+)-N-allylnormetazocine ((+)-SKF 10,047), at doses of 100 to 300 micrograms/kg, but not with (-)-SKF 10,047. DTG, at the same dose range that reversed the decrease in alternation, also totally reversed the CO-induced decrease in step-down latency in the passive avoidance test. The curve for these effects was bell-shaped; the effects were not observed at the dose of 1 mg/kg. Moreover, alpha-(4-fluorophenyl-2-pyrimidinyl)-1-piperazine butanol (BMY 14802), a putative sigma antagonist (1-10 mg/kg i.p.), did not affect CO-induced amnesia, but when simultaneously administered with DTG, it completely prevented its effect in both tests.(ABSTRACT TRUNCATED AT 250 WORDS)
CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
*Amnesia: CI, chemically induced
*Amnesia: DT, drug therapy
Amnesia: PP, physiopathology
*Behavior, Animal: PH, physiology
*Carbon Monoxide
Dose-Response Relationship, Drug
Guanidines: TU, therapeutic use
***Ligands**
Memory: DE, drug effects
*Memory: PH, physiology
Mice
***Receptors, sigma: PH, physiology**

L17 ANSWER 12 OF 70 MEDLINE
AN 94349129 MEDLINE
TI Behavioral evidence for a modulating role of sigma ligands in memory processes. I. Attenuation of dizocilpine (MK-801)-induced amnesia.
AU Maurice T; Hiramatsu M; Itoh J; Kameyama T; Hasegawa T; Nabeshima T
CS Department of Neuropsychopharmacology and Hospital Pharmacy, Nagoya University School of Medicine, Japan..
SO BRAIN RESEARCH, (1994 May 30) 647 (1) 44-56.
Journal code: B5L. ISSN: 0006-8993.

CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9412
AB The potentiating effect of low doses of sigma ligands on the N-methyl-D-aspartate (NMDA)-induced excitation of pyramidal CA3 dorsal hippocampal neurons has recently been reported. In the present study, we investigated behavioral effects relevant to these findings in the experimental amnesia induced by the non-competitive NMDA antagonist, dizocilpine (MK-801), in mice. At doses below 1 mg/kg s.c., the sigma ligands, 1,3-di-(2-tolyl)guanidine (DTG), (+)-SKF 10,047, and (+)-pentazocine, but not their (-)-isomers, significantly decreased MK-801 (100 microgram/kg s.c.)-induced impairment of spontaneous alternation performances in 8-min sessions of a Y-maze exploration, an index of spatial working memory, without affecting the concomitant hyperlocomotion. The effect of DTG (100 micrograms/kg s.c.) was completely antagonized by the simultaneous administration of BMY 14802 (10 mg/kg i.p.) and NE-100 (1 mg/kg i.p.), two putative sigma antagonists, which had no effect by themselves. In long-term memory tests (step-down and step-through types of passive avoidance, elevated plus-maze), DTG exhibited a significant attenuation of MK-801-induced amnesia, at doses of 10 and 100 micrograms/kg s.c. In all tests of short- and long-term memory, the effects exhibited by the sigma ligands tested had a bell-shaped curve; no effect was seen at 1 mg/kg. DTG did not affect the impairment of alternation induced by CPP (5 mg/kg i.p.): the modulation may selectively target the blockade of NMDA receptor-associated ion channels. Moreover, DTG (1-1000 micrograms/kg) did not affect the impairment induced by scopolamine (1 mg/kg i.p.) or diazepam (4 mg/kg i.p.), but significantly prevented the impairment induced by mecamylamine (10 mg/kg i.p.). These results suggest that the potentiating effect of sigma ligands on NMDA receptor-mediated glutamatergic neurotransmission, already demonstrated electrophysiologically, may have some relevance to learning and memory processes in the hippocampus. A similar modulation may also affect cholinergic nicotinic systems.
CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
*Amnesia: CI, chemically induced
*Amnesia: PP, physiopathology
*Behavior, Animal: PH, physiology
*Dizocilpine Maleate
Guanidines: PD, pharmacology
***Ligands**
Memory: DE, drug effects
*Memory: PH, physiology
Mice
***Receptors, sigma: PH, physiology**

L17 ANSWER 13 OF 70 MEDLINE

AN 94020083 MEDLINE
TI Behavioural effect of pretreatment with **opioid** antagonists and sigma binding site **ligands** on the abnormal motor response produced by the kappa **opioid** agonist U50,488H in guinea pigs.
AU Brent P J
CS Neuropharmacology Laboratory, Mater Hospital Waratah 2298, Faculty of Medicine, University of Newcastle, NSW, Australia..
SO NEUROPHARMACOLOGY, **(1993 Aug)** 32 (8) 751-60.
Journal code: NZB. ISSN: 0028-3908.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9401
AB Dose-responsive motor activity induced by systemic injection of the kappa (kappa) preferring opioid agonist, U50,488H (1-10 mg/kg, s.c.) in guinea pigs was recently reported [Brent P. J. and Bot G. (1992) Psychopharmacology 107: 581-590], characterised at the higher doses used (5-10 mg/kg) by sustained postural abnormalities. The effects on the U50,488H-induced, abnormal, motor response of pharmacological manipulation of opioid receptors and sigma (sigma) sites was studied. The opioid antagonist naloxone, [5 and 15 mg/kg, subcutaneously (s.c.)], the kappa selective antagonist, norbinaltorphimine (NBNI), administered intracerebroventricularly (i.c.v., 20 and 50 nM) 0.5 hr before U50,488H, and the anticonvulsant phenytoin [25 and 50 mg/kg, intraperitoneally (i.p.)] given 1 hr before, attenuated the abnormal postures, whereas naloxone methobromide (15 mg/kg), a quaternary opioid which does not cross the blood-brain barrier, had no significant effect on the movements. In contrast, the drugs with varying affinity for sigma binding sites such as 1,3-di(2-tolyl)guanidine (DTG, 10 and 30 mg/kg), haloperidol (1 and 5 mg/kg, s.c.), dextromethorphan (1, 10 and 20 mg/kg, s.c.) and reduced haloperidol (1 mg/kg, s.c.), given 0.5-1 hr before U50,488H, exacerbated the severity of the abnormal motor activity in a dose-related manner by decreasing the latency to onset of maximum obtainable motor response and increasing the duration of the response. In addition, haloperidol (1 and 5 mg/kg, s.c.), dextromethorphan (10 mg/kg, s.c.) and DTG (30 mg/kg, s.c.), given in combination with U50,488H, induced behaviour characterised by marked oral activity. In contrast to the effect of haloperidol, pretreatment with the selective dopamine D-2 antagonist, raclopride (10 mg/kg, s.c.), had no significant effect on the abnormal movements induced by U50,488H, but did induce oral activity. These data indicate the possible involvement of kappa opioid receptors in the abnormal movement induced by U50,488H, and further demonstrate that there is an interaction between the kappa receptors and sigma sites which can influence the abnormal motor activity.
CT Check Tags: Animal; Female; Male; Support, Non-U.S. Gov't
*Analgesics: PD, pharmacology

*Behavior, Animal: DE, drug effects
Dose-Response Relationship, Drug
Drug Interactions
Guinea Pigs
Injections, Intraventricular
Ligands
*Locomotion: DE, drug effects
Motor Activity: DE, drug effects
*Narcotic Antagonists: PD, pharmacology
Phenytoin: PD, pharmacology
Posture
*Pyrrolidines: PD, pharmacology
***Receptors, sigma: DE, drug effects**
Receptors, Dopamine D2: AI, antagonists & inhibitors
Receptors, Dopamine D2: ME, metabolism
***Receptors, Opioid, kappa: DE, drug effects**
Salicylamides: PD, pharmacology

L17 ANSWER 14 OF 70 MEDLINE
AN 93382274 MEDLINE
TI Photoaffinity **ligands** for the mu **opioid** receptor.
AU Simon E J; Fan L Q; Hiller J M; Seyed-Mozaffari A; Schultz A G; Archer S
CS Department of Psychiatry and Pharmacology, New York University Medical Center, NY 10016..
NC DA-01674 (NIDA)
SO LIFE SCIENCES, **(1993)** 53 (14) 1173-8.
Journal code: L62. ISSN: 0024-3205.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9312
AB Two affinity ligands, 6 beta-(5-Azido-2-nitrophenacetamido) 14 beta-hydroxy-7,8-dihydromorphinone (4) and 6 beta-(5-azido-2-nitrophenacetamido) 14 beta-hydroxy-7,8-dihydro-N-cyclopropylmethylnormorphinone (5) bind reversibly to opioid receptors present in bovine caudate membranes and photolyse in a range of wavelengths centered about 366 nm to produce wash-resistant binding to the mu receptor. At these wavelengths very little if any photodestruction of the mu receptor occurs over the 20 minute period of irradiation at 0 degree C.
CT Check Tags: Animal; In Vitro; Male; Support, U.S. Gov't, P.H.S.
*Affinity Labels: ME, metabolism
*Azides: ME, metabolism
Cattle
Guinea Pigs
Ligands
*Morphine Derivatives: ME, metabolism

Photochemistry
***Receptors, Opioid, mu: ME, metabolism**

L17 ANSWER 15 OF 70 MEDLINE
AN 93380575 MEDLINE
TI cDNA cloning and pharmacological characterization of an **opioid** receptor with high affinities for kappa-subtype-selective **ligands**.
AU Nishi M; Takeshima H; Fukuda K; Kato S; Mori K
CS International Institute for Advanced Studies, Kyoto, Japan..
SO FEBS LETTERS, **(1993 Sep 6)** 330 (1) 77-80.
Journal code: EUH. ISSN: 0014-5793.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-D16534
EM 9312
AB The amino acid sequence of a rat opioid receptor, designated as ROR-D, has been deduced by cloning and sequencing the cDNA. The ROR-D expressed from the cDNA exhibits high affinities for ligands selective for the opioid receptor kappa-subtype and low affinities for ligands selective for the delta- and mu-subtypes. RNA blot hybridization analysis indicated that ROR-D mRNA is distributed in cerebrum and brainstem but not in cerebellum.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Amino Acid Sequence
Brain: ME, metabolism
Cells, Cultured
Cloning, Molecular
DNA
Ligands
Molecular Sequence Data
Rats
Rats, Wistar
Receptors, Opioid, delta: DE, drug effects
Receptors, Opioid, delta: ME, metabolism
Receptors, Opioid, kappa: DE, drug effects
***Receptors, Opioid, kappa: GE, genetics**
Receptors, Opioid, kappa: ME, metabolism
Receptors, Opioid, mu: DE, drug effects
Receptors, Opioid, mu: ME, metabolism
Sequence Homology, Amino Acid

L17 ANSWER 16 OF 70 MEDLINE
AN 93312462 MEDLINE
TI Synthesis and **opioid** receptor affinity of bivalent **ligands** derived from 3,8-diazabicyclo(3.2.1)octanes.
AU Barlocco D; Fadda P; Fratta W
CS 1st. Chim. Farm. E Toss., Universit`a di Milano, Italy..

SO FARMACO, **(1993 Mar)** 48 (3) 387-96.
Journal code: ACZ. ISSN: 0014-827X.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9310
AB A new series of bivalent ligands (2a-d), derived from the previously reported analgesic 3-cinnamyl-8-propionyl-3,8-diazabicyclo(3.2.1)octane (1a), has been synthesized and tested in vitro for their affinity towards opioid receptors and in vivo for their analgesic potency. None of the new compounds showed either appreciable affinity for opioid receptors or analgesic activity comparable to that of the model 1a.
CT Check Tags: Animal; In Vitro; Male
*Analgesics: CS, chemical synthesis
Analgesics: PD, pharmacology
*Bicyclo Compounds: CS, chemical synthesis
Bicyclo Compounds: PD, pharmacology
Binding, Competitive: DE, drug effects
Brain: ME, metabolism
Chemistry, Physical
Ligands
Mice
Morphine: PD, pharmacology
Pain Measurement: DE, drug effects
Rats
Rats, Sprague-Dawley
***Receptors, Opioid: ME, metabolism**
Receptors, Opioid, delta: ME, metabolism
Receptors, Opioid, kappa: ME, metabolism
Receptors, Opioid, mu: ME, metabolism

L17 ANSWER 17 OF 70 MEDLINE
AN 93294799 MEDLINE
TI Non-peptide **ligands** for **opioid** receptors. Design of kappa-specific agonists.
AU Ronsisvalle G; Pasquinucci L; Pappalardo M S; Vittorio F; Fronza G; Romagnoli C; Pistacchio E; Spampinato S; Ferri S
CS Istituto di Chimica Farmaceutica e Tossicologica, Universit`a di Catania, Italy.
SO JOURNAL OF MEDICINAL CHEMISTRY, **(1993 Jun 25)** 36 (13) 1860-5.
Journal code: J0F. ISSN: 0022-2623.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9309
AB A series of phenyl carboxyl esters 5a-d derived from

N-(cyclopropylmethyl)normetazocine was synthesized and evaluated for its selectivity at mu, kappa, and delta opioid receptors. Compound 5a, although 43 times less potent than the reference compound U50488, was specific for kappa receptors, having no detectable affinity for either mu or delta receptors. Greater binding affinity was seen with the diastereoisomer having the 1'R,2'S stereochemistry in the cyclopropyl ring of the nitrogen substituent, which was only 12 times less active than U50488. Antinociceptive activity in the mouse tail flick was only slightly lower than that of U50488 (ED50 = 7.66 vs 4.52 mg/kg). Naloxone fully prevented antinociception induced by (1'R,2'S)-5a at the doses of 2.0 mg/kg. Compound (1'R,2'S)-5a is one of the most kappa-selective non-peptide compounds reported to date. The implications of these results in terms of requirements for kappa ligands are discussed.

CT Check Tags: Animal; In Vitro; Male; Support, Non-U.S. Gov't
Brain: ME, metabolism
*Cyclazocine: AA, analogs & derivatives
Cyclazocine: CS, chemical synthesis
Cyclazocine: ME, metabolism
Cyclazocine: PD, pharmacology
Drug Design
Esters: CS, chemical synthesis
Esters: PD, pharmacology
Guinea Pigs
Hydrogen Bonding
Ligands
Mice
Models, Molecular
Molecular Conformation
Rats
Rats, Sprague-Dawley
***Receptors, Opioid, kappa: DE, drug effects**
Receptors, Opioid, kappa: ME, metabolism
Stereoisomerism
Structure-Activity Relationship

L17 ANSWER 18 OF 70 MEDLINE
AN 93101628 MEDLINE
TI Differential stereochemical requirements of mu vs. delta **opioid** receptors for **ligand** binding and signal transduction: development of a class of potent and highly delta-selective peptide antagonists.
AU Schiller P W; Nguyen T M; Weltrowska G; Wilkes B C; Marsden B J; Lemieux C; Chung N N
CS Laboratory of Chemical Biology and Peptide Research, Clinical Research Institute of Montreal, PQ, Canada..
NC DA-06252 (NIDA)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1992 Dec 15)** 89 (24) 11871-5.
Journal code: PV3. ISSN: 0027-8424.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9303
AB Opioid peptide analogs consisting entirely of aromatic amino acid residues and containing conformationally restricted phenylalanine derivatives in position 2 of the peptide sequence were synthesized and pharmacologically characterized in vitro. Both diastereoisomers of H-Tyr-(D or L)-NMePhe-Phe-Phe-NH2 (NMePhe is N alpha-methylphenylalanine) were mu-receptor-selective, were full agonists in the mu-receptor-representative guinea pig ileum assay, and were partial agonists in the mouse vas deferens assay, with the L-NMePhe2 analog displaying somewhat higher intrinsic activity than the D-NMePhe2 analog. Further conformational restriction at position 2 in the sequence, as achieved through substitution of D- or L-tetrahydro-3-isoquinoline carboxylic acid (Tic), produced a configuration-dependent differential effect on receptor selectivity and intrinsic activity, leading to a potent mu-selective mu agonist (the D-Tic2 analog) with increased intrinsic activity in the mouse vas deferens assay and to a potent delta-selective delta antagonist (the L-Tic2 analog). These results demonstrate that imposition of conformational constraints in a peptide not only may alter receptor selectivity but also may decrease, totally abolish, or even enhance intrinsic activity. The tetrapeptide H-Tyr-Tic-Phe-Phe-NH2 was a moderately potent full agonist in the guinea pig ileum assay and, thus, represents a compound with mixed mu-agonist/delta-antagonist properties. The corresponding peptide with a free C-terminal carboxyl group H-Tyr-Tic-Phe-Phe-OH showed high delta-receptor affinity (Ki delta = 1.2 nM), unprecedented delta selectivity (Ki mu/Ki delta = 1410), high potency as delta antagonist (Ke = 3-8 nM against various delta agonists in the mouse vas deferens assay) and, unlike other delta antagonists, had no mu-antagonist properties. The tripeptides H-Tyr-Tic-Phe-OH and H-Tyr-Tic-Phe-NH2 were also delta antagonists.
CT Check Tags: Animal; In Vitro; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Biological Assay
Guinea Pigs
Ligands
Mice
Models, Molecular
Molecular Sequence Data
*Oligopeptides: CH, chemistry
Oligopeptides: ME, metabolism
Protein Conformation
***Receptors, Opioid, delta: ME, metabolism**
***Receptors, Opioid, mu: ME, metabolism**
Structure-Activity Relationship

L17 ANSWER 19 OF 70 MEDLINE
AN 93063211 MEDLINE
TI **Opiate** total synthesis and contemporary NIDDK analgesic research-natural and unnatural **ligands** for computed tomography imaging of receptors in conscious humans. Implications for future advances in the neurosciences.
AU Rice K C
CS Laboratory of Medicinal Chemistry, National Institute of Diabetes, Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD 20892..
SO NIDA RESEARCH MONOGRAPH, **(1992)** 119 91-5. Ref: 0
Journal code: NRM. ISSN: 1046-9516.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 9302
CT Check Tags: Animal; Human
*Analgesics: CS, chemical synthesis
Analgesics: PD, pharmacology
*Endorphins: CS, chemical synthesis
Endorphins: PD, pharmacology
Ligands
National Institutes of Health (U.S.)
*Neurology
***Receptors, Opioid: DE, drug effects**
Research
Tomography, X-Ray Computed
United States

L17 ANSWER 20 OF 70 MEDLINE
AN 92367154 MEDLINE
TI Acute effects of sigma ligands on the electrophysiological activity of rat nigrostriatal and mesoaccumbal dopaminergic neurons.
AU Zhang J; Chiodo L A; Wettstein J G; Junien J L; Freeman A S
CS Department of Psychiatry, Wayne State University School of Medicine, Detroit, Michigan 48201..
NC MH42136 (NIMH)
DA07844 (NIDA)
MH41557 (NIMH)
SO SYNAPSE, (1992 Aug) 11 (4) 267-78.
Journal code: VFL. ISSN: 0887-4476.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9211

AB The effects of acute i.v. administration of several sigma ligands on the single-unit activity of nigrostriatal and mesoaccumbal dopaminergic (DA) neurons were evaluated in chloral hydrate-anesthetized rats. DTG (1,3-di(o-tolyl)guanidine) did not alter DA neuronal activity at nontoxic doses and JO 1784 [(+)-N-cyclopropylmethyl-N-methyl-1,4-diphenyl-1-ethylbut-3-en-1-+ ++ylamine] was inactive. (+)-Pentazocine was more effective in increasing mesoaccumbal vs. nigrostriatal DA cell firing rates. BMY 14802(alpha-(4-fluorophenyl)-4-(5-fluoro-2-pyrimidinyl)-1-piperazine-but anol) dose-dependently increased DA cell firing rate in both populations. The inhibition of nigrostriatal DA cell firing rate by (+)-3-(3-hydroxyphenyl)-N-(1-propyl)piperidine [(+)-3-PPP] was reversed by (-)-eticlopride and (+)-but not (-)-butaclamol, which supports previous evidence that (+)-3-PPP-induced inhibition is due to the DA agonist properties of the drug. From what is known of the pharmacological properties of these compounds, it is concluded that acute sigma receptor occupation does not markedly alter the firing rate of DA neurons. The dose-response curve for inhibition of nigrostriatal DA neuronal activity by the D2 DA agonist, quinpirole, was shifted to the right tenfold by BMY 14802 pretreatment (8 mg/kg, i.v.) and twofold by (+)-pentazocine (8 mg/kg, i.v.), but was not changed by DTG (2 mg/kg, i.v.). It is concluded that the marked effects of certain sigma ligands on DA cell electrophysiology are likely due to their non-sigma properties.

CT Check Tags: Animal; Male; Support, U.S. Gov't, P.H.S.
Caudate Nucleus: CY, cytology
Caudate Nucleus: DE, drug effects
*Caudate Nucleus: PH, physiology
*Dopamine: PH, physiology
Electrophysiology
***Ligands**
Neurons: DE, drug effects
*Neurons: PH, physiology
Putamen: CY, cytology
Putamen: DE, drug effects
*Putamen: PH, physiology
Rats
Rats, Inbred Strains
***Receptors, Opioid: ME, metabolism**
Substantia Nigra: CY, cytology
Substantia Nigra: DE, drug effects
*Substantia Nigra: PH, physiology

L17 ANSWER 21 OF 70 MEDLINE
AN 92333305 MEDLINE
TI Differential effects of Mg2+ and other divalent cations on the binding of tritiated **opioid ligands**.
AU Rodriguez F D; Bardaji E; Traynor J R
CS Department of Chemistry, University of Technology, Loughborough, Leicestershire, England.

SO JOURNAL OF NEUROCHEMISTRY, **(1992 Aug)** 59 (2) 467-72.
Journal code: JAV. ISSN: 0022-3042.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9210

AB The effects of MgCl2 on the binding of tritiated ligands to opioid binding sites in homogenates of guinea-pig brain in HEPES buffer have been studied. The binding of tritiated mu-, delta-, and kappa-opioid agonists was promoted in a concentration-dependent manner over a range of MgCl2 concentrations from 0.1 mM to 10 mM, as was binding of the nonselective antagonists [3H]diprenorphine and [3H]naloxone. At concentrations of MgCl2 above 10 mM reversal of this effect was observed. The effects of MgCl2 on binding parameters differed at each site. The promoting effects of MgCl2 were mimicked by MnCl2, CaCl2, and MgSO4, but CoCl2 and ZnCl2 were inhibitory. Following treatment of guinea-pig brain synaptosomes at pH 11.5 to eliminate G proteins, the binding of the mu-opioid agonist [3H][D-Ala2, MePhe4, Gly-ol5]enkephalin and [3H]naloxone was much reduced but binding of [3H]diprenorphine was unaffected. Under these conditions MgCl2 still promoted binding of [3H]diprenorphine. The results suggest that Mg2+ ions promote binding by an action at the opioid receptor, even in the absence of G protein, and that opioid antagonists may differ in their recognition of opioid receptor binding sites.

CT Check Tags: Animal; Comparative Study; Male; Support, Non-U.S. Gov't
Calcium: PD, pharmacology
Cations, Divalent: PD, pharmacology
Cobalt: PD, pharmacology
Diprenorphine: ME, metabolism
Dose-Response Relationship, Drug
*Endorphins: ME, metabolism
Guinea Pigs
Hydrogen-Ion Concentration
Ligands
*Magnesium: PD, pharmacology
Manganese: PD, pharmacology
Naloxone: ME, metabolism
Rats
Rats, Inbred Strains
Receptors, Opioid: DE, drug effects
Receptors, Opioid: ME, metabolism
Synaptic Membranes: ME, metabolism
Synaptic Membranes: UL, ultrastructure
Synaptosomes: ME, metabolism
Synaptosomes: UL, ultrastructure
Tritium
Zinc: PD, pharmacology

L17 ANSWER 22 OF 70 MEDLINE
AN 92318206 MEDLINE
TI Electrophilic **opioid ligands**. Oxygen tethered alpha-methylene-gamma-lactone, acrylate, isothiocyanate, and epoxide derivatives of 6 beta-naltrexol.
AU Dasher W E; Klein P; Nelson W L
CS Department of Medicinal Chemistry, School of Pharmacy, University of Washington, Seattle 98195.
NC DA-03933 (NIDA)
DA-06675 (NIDA)
SO JOURNAL OF MEDICINAL CHEMISTRY, **(1992 Jun 26)** 35 (13) 2374-84.
Journal code: J0F. ISSN: 0022-2623.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9210
AB O6-Ether derivatives of 6 beta-naltrexol in which the ether substituent includes various electrophilic groups have been synthesized in an effort to examine structure-activity requirements at the 6 beta-substituent for receptor affinity and irreversibility of binding in opioid receptor preparations. A series of tethered 6 beta-ethers having terminal epoxides, alpha-methylene-gamma-lactones, and an isothiocyanate group were prepared. The stereochemistry of the alpha-methylene-gamma-lactones was established by convergent synthesis of their reduction products from epoxides of known absolute stereochemistry. In general, the tested compounds showed comparable affinity and selectivity for the receptor subtypes. All were found with high affinity for mu-sites. The terminal epoxide ether diastereomers 8 and 9 were not bound irreversibly in the assay for total opioid receptors. The alpha-methylene-gamma-lactone diastereomers 10 and 11, and their O14-acetyl precursors 20 and 21, respectively, varied in their irreversible effects, but where noted these effects were mu-site selective. Methacrylate ether 7 and isothiocyanate ether 12 were bound irreversibly at both mu- and delta-sites.
CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
Acrylates: CH, chemistry
Binding Sites
Brain: ME, metabolism
*Endorphins: ME, metabolism
Epoxy Compounds: CH, chemistry
Guinea Pigs
Lactones: CH, chemistry
Ligands
*Naltrexone: AA, analogs & derivatives
Naltrexone: CH, chemistry
Radioligand Assay
Receptors, Opioid: ME, metabolism

Stereoisomerism
Thiocyanates: CH, chemistry

L17 ANSWER 23 OF 70 MEDLINE
AN 92182940 MEDLINE
TI Effects of sigma ligands on mouse cerebellar cyclic guanosine monophosphate (cGMP) levels in vivo: further evidence for a functional modulation of N-methyl-D-aspartate (NMDA) receptor complex-mediated events by sigma ligands.
AU Rao T S; Mick S J; Cler J A; Emmett M R; Dilworth V M; Contreras P C; Gray N M; Wood P L; Iyengar S
CS Searle Research and Development, G.D. Searle-Monsanto Co., St. Louis, MO 63198..
SO BRAIN RESEARCH, (1991 Oct 4) 561 (1) 43-50.
Journal code: B5L. ISSN: 0006-8993.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9206
AB In the present investigation, the effects of sigma ligands [WY-47384 [8-fluoro-2,3,4,5-tetrahydro-2[3-(3-pyridinyl)propyl)1H-pyrido(4,3b)indole], (+)-pentazocine, (+)-SFK 10,047 (N-allylnormetazocine), mafoprazine, opipramol, dextromethorphan, dextrorphan, (+)-3-PPP [3-(3-hydroxyphenyl)-N-propylpiperidine], (-)-butaclamol, DTG [1,3-di(2-tolyl)guanidine], rimcazole, ifenprodil and BMY-14802 [alpha-(fluorophenyl)-4-(5-fluoropyrimidinyl)-1-piperazine butanol]] on harmaline-, pentylenetetrazol (PTZ)-, methamphetamine (MA)- and D-serine-induced increases in mouse cerebellar levels of cGMP were determined. Ifenprodil, BMY-14802, dextromethorphan, dextrorphan, (+)-SKF 10,047, opipramol and mafoprazine reversed harmaline-, PTZ-, MA- and D-serine-induced increases in levels of cGMP. Rimcazole reversed only the harmaline-induced response. WY-47384 reversed harmaline-, MA-, D-serine-, but not PTZ- or quisqualate-induced increases in levels of cGMP. (+)-Pentazocine attenuated harmaline- and D-serine-, but not PTZ- and MA-induced cGMP responses. Haloperidol did not affect harmaline- and D-serine-induced cGMP responses. (+)-3-PPP and (-)-butaclamol did not affect any of the responses studied. Furthermore, (+)-3-PPP-induced increases in levels of cGMP were reversed by the competitive N-methyl-D-aspartate (NMDA) antagonist, CPP]3-(2-carboxypiperazin-4-yl)propyl- 1-phosphonic acid, the non-competitive NMDA antagonist, (+)-MK-801 (dizocilipine maleate), the NMDA-associated glycine receptor antagonist, HA-966 (3-amino-1-hydroxypyrrolidin-2-one), the partial glycine agonist, DCS (D-cycloserine) as well as by the sigma ligands, ifenprodil, WY-47384, (+)-pentazocine, (+)-SKF 10,047, dextromethorphan and dextrorphan but not by rimcazole.(ABSTRACT TRUNCATED AT 250 WORDS)
CT Check Tags: Animal; Male
*Cerebellum: ME, metabolism

*Cyclic GMP: ME, metabolism
Dopamine Agents: AI, antagonists & inhibitors
Harmaline: AI, antagonists & inhibitors
***Ligands**
Methamphetamine: AI, antagonists & inhibitors
Mice
Pentylenetetrazole: AI, antagonists & inhibitors
Piperidines: AI, antagonists & inhibitors
Quisqualic Acid: AI, antagonists & inhibitors
*Receptors, N-Methyl-D-Aspartate: DE, drug effects
***Receptors, Opioid: DE, drug effects**
Serine: AI, antagonists & inhibitors

L17 ANSWER 24 OF 70 MEDLINE
AN 92158819 MEDLINE
TI 125I][D-Ala2]deltorphin-I: a high affinity, delta-selective **opioid** receptor **ligand**.
AU Dupin S; Tafani J A; Mazarguil H; Zajac J M
CS Laboratoire de Pharmacologie et de Toxicologie Fondamentales, CNRS, Toulouse, France..
SO PEPTIDES, **(1991 Jul-Aug)** 12 (4) 825-30.
Journal code: PA7. ISSN: 0196-9781.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9205
AB The selective delta opioid agonist [D-Ala2]deltorphin-I was radioiodinated and the product purified using reverse phase HPLC. The binding characteristics and distribution profile of [125I][D-Ala2]deltorphin-I were assessed in mouse brain using homogenate binding techniques and quantitative autoradiography. [125I][D-Ala2]deltorphin-I bound with high affinity to a single class of sites (KD = 0.5 nM) in brain membrane preparations and striatal sections. Competition studies indicated that [125I][D-Ala2]deltorphin-I was selectively labeling delta opioid receptors as shown by the ratio of apparent affinities for mu and delta receptors (KI mu/KI delta = 1388). The autoradiographical distribution profile of [125I][D-Ala2]deltorphin-I binding sites was also consistent with that of other delta-selective radioligands. The data indicate that [125I][D-Ala2]deltorphin-I binds to delta opioid receptors with high affinity and selectivity. Because of its very high specific activity, it can be detected rapidly with high sensitivity by autoradiographic emulsion.
CT Check Tags: Animal; Male
Amino Acid Sequence
Autoradiography
Brain: ME, metabolism
Chromatography, High Pressure Liquid
Enkephalins: PD, pharmacology

FK 33-824: AI, antagonists & inhibitors
FK 33-824: ME, metabolism
Iodine Radioisotopes
Ligands
Mice
Molecular Sequence Data
*Oligopeptides: ME, metabolism
***Receptors, Opioid: ME, metabolism**
Substrate Specificity

L17 ANSWER 25 OF 70 MEDLINE
AN 91347449 MEDLINE
TI Pharmacological study on an irreversible **ligand** of **opioid** receptors, A-alpha-CAM, and its reaction with the sulfhydryl group.
AU Ye C
CS Institute of Basic Medical Sciences, Beijing..
SO CHUNG-KUO I HSUEH KO HSUEH YUAN HSUEH PAO ACTA ACADEMIAE MEDICINAE SINICAE, **(1991 Feb)** 13 (1) 39-45.
Journal code: CZS. ISSN: 1000-503X.
CY China
DT Journal; Article; (JOURNAL ARTICLE)
LA Chinese
EM 9112
AB A-alpha-CAM is an irreversible partial agonist of opiate receptors. Its binding to opioid receptors from P2 membrane preparations of rat brain and its effect on isolated tissues (GPI, MVD, RVD and RbVD) could not be washed away, indicating the irreversible nature of its binding. A-alpha-CAM inhibited the electrically elicited contraction of GPI, a pure agonist, with an IC50 of 2.6 mumol/L, and this effect could not be antagonized by Nx. A-alpha-CAM acted as a partial agonist on MVD with an IC50 of 0.153 mumol/L. With RVD and RbVD, A-alpha-CAM acted as an antagonist with PA2 values of 7.4 and 7.7 respectively. Possibly, covalent binding of A-alpha-CAM with the sulfhydryl groups of opioid receptors is the biochemical mechanisms responsible for its irreversible action.
CT Check Tags: Animal; Male
Binding Sites
English Abstract
Guinea Pigs
Ileum: DE, drug effects
Ligands
Mice
*Muscle Contraction: DE, drug effects
*Muscle, Smooth: DE, drug effects
Muscle, Smooth: PH, physiology
Rabbits
Rats
***Receptors, Opioid: DE, drug effects**
*Thebaine: AA, analogs & derivatives

Thebaine: PD, pharmacology
Vas Deferens: DE, drug effects

L17 ANSWER 26 OF 70 MEDLINE
AN 91318909 MEDLINE
TI Delta **opioid** receptor-selective **ligands**: [D-Pen2,D-Pen5]enkephalin-dermenkephalin chimeric peptides.
AU Cavagnero S; Misicka A; Knapp R J; Davis P; Fang L; Burks T F; Yamamura H I; Hruby V J
CS Department of Chemistry, University of Arizona, Tucson 85721..
NC DA 06284 (NIDA)
NS 19972 (NINDS)
SO LIFE SCIENCES, **(1991)** 49 (7) 495-503.
Journal code: L62. ISSN: 0024-3205.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9111
AB A number of DPDPE-dermenkephalin chimeric peptides have been synthesized in which the putative C-terminal delta-address of dermenkephalin has been linked to the highly delta opioid selective cyclic peptide [D-Pen2,D-Pen5]enkephalin (DPDPE). Asp, Met-Asp and Leu-Met-Asp have been added to the C-terminus of DPDPE and both the carboxyl terminal and the carboxamide terminal series have been prepared. The bioassays using the mouse vas deferens and guinea pig ileum preparations have revealed a steady decrease in potency (compared to DPDPE) at delta and mu receptors as the dermenkephalin sequences were added. Some of the analogues, however, retained high delta selectivity. Similar results were obtained using radioligand binding assays. These findings suggest that the C-terminal amino acid sequence of dermenkephalin plays a role of delta-address which is specific to dermenkephalin itself, and is not additive with another delta selective ligand such as DPDPE.
CT Check Tags: Animal; Male; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Chimera
Enkephalins: ME, metabolism
Guinea Pigs
Ligands
Mice
Mice, Inbred ICR
Molecular Sequence Data
*Oligopeptides: ME, metabolism
Peptides, Cyclic: CS, chemical synthesis
*Peptides, Cyclic: ME, metabolism
Radioligand Assay
Rats
Rats, Inbred Strains

***Receptors, Opioid: ME, metabolism**
Structure-Activity Relationship

L17 ANSWER 27 OF 70 MEDLINE
AN 91202479 MEDLINE
TI Role of the spacer in conferring kappa **opioid** receptor selectivity to bivalent **ligands** related to norbinaltorphimine.
AU Portoghese P S; Garzon-Aburbeh A; Nagase H; Lin C E; Takemori A E
CS Department of Medicinal Chemistry, College of Pharmacy, University of Minnesota, Minneapolis 55455.
SO JOURNAL OF MEDICINAL CHEMISTRY, **(1991 Apr)** 34 (4) 1292-6.
Journal code: J0F. ISSN: 0022-2623.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9107
AB The thiophene 2 and pyran 3 analogues of the kappa-selective opioid antagonist norbinaltorphimine (1a, norBNI) were synthesized and tested in an effort to determine the contribution of the spacer to the interaction of bivalent ligands at different opioid receptor types. Both 2 and 3 were found to be selective kappa opioid receptor antagonists in smooth muscle preparations, and they bound selectively to kappa-recognition sites. The thiophene analogue 2 displayed binding selectivity that was of the same order of magnitude as that of 1a, while 3 was considerably less selective for kappa site. This is consistent with the fact that the second pharmacophore in 1a and 2 displayed a greater degree of superposition than 1a and 3. The results of this study suggest that the pyrrole moiety of norBNI functions primarily as an inert spacer to rigidly hold the basic nitrogen in the second pharmacophore at an "address" subsite that is unique for the kappa opioid receptor.
CT Check Tags: Animal; In Vitro; Male; Support, U.S. Gov't, P.H.S.
Binding, Competitive
Indicators and Reagents
Kinetics
Ligands
Molecular Conformation
Molecular Structure
*Muscle Contraction: DE, drug effects
Muscle, Smooth: DE, drug effects
Muscle, Smooth: PH, physiology
*Naltrexone: AA, analogs & derivatives
*Naltrexone: CS, chemical synthesis
Naltrexone: PD, pharmacology
Receptors, Opioid: DE, drug effects
***Receptors, Opioid: ME, metabolism**
Structure-Activity Relationship

L17 ANSWER 28 OF 70 MEDLINE
AN 91156110 MEDLINE
TI **Opipramol**, a potent sigma **ligand**, is an anti-ischemic agent: neurochemical evidence for an interaction with the N-methyl-D-aspartate receptor complex in vivo by cerebellar cGMP measurements.
AU Rao T S; Cler J A; Mick S J; Ragan D M; Lanthorn T H; Contreras P C; Iyengar S; Wood P L
CS CNS Diseases Research, G.D. Searle & Co., Monsanto Company, St Louis, Missouri 63198..
SO NEUROPHARMACOLOGY, **(1990 Dec)** 29 (12) 1199-204.
Journal code: NZB. ISSN: 0028-3908.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9106
AB Opipramol, a potent sigma ligand and a tricyclic antidepressant compound, provided significant neuronal protection (P less than 0.0001) against ischemia-induced neuronal cell loss in the hippocampus in Mongolian gerbils, at a dose of 50 mg/kg (30 min pretreatment). However, opipramol did not offer protection when given 60 min after the ischemic insult. Opipramol decreased basal levels of cGMP in the cerebellum of the mouse and harmaline-induced increases in levels of cGMP, with approximate ED50 values of 4 and 27 mg/kg. Opipramol antagonized methamphetamine- and pentylenetetrazol-induced increases in levels of cGMP. Parenteral administration of opipramol also antagonized the increases in levels of cGMP in the cerebellum of the mouse after the local administration of D-serine, an agonist at the N-methyl-D-aspartate (NMDA)-associated, strychnine-insensitive glycine receptor. These results indicate that opipramol attenuates responses mediated through the NMDA receptor complex. These results further support the functional modulation of the NMDA receptor complex by sigma ligands and provide a neurochemical correlate for the observed anti-ischemic properties of opipramol.
CT Check Tags: Animal; Male
Cerebellum: DE, drug effects
*Cerebellum: ME, metabolism
Cerebral Ischemia, Transient: PA, pathology
*Cerebral Ischemia, Transient: PC, prevention & control
Cyclic GMP: ME, metabolism
Gerbillinae
Hippocampus: DE, drug effects
*Hippocampus: PA, pathology
Ligands
Methamphetamine: PD, pharmacology
Mice
Neurons: DE, drug effects
*Neurons: PA, pathology

Opipramol: PD, pharmacology
*Opipramol: TU, therapeutic use
Pentylenetetrazole: PD, pharmacology
Receptors, N-Methyl-D-Aspartate: DE, drug effects
*Receptors, N-Methyl-D-Aspartate: PH, physiology
Receptors, Opioid: DE, drug effects
***Receptors, Opioid: PH, physiology**

L17 ANSWER 29 OF 70 MEDLINE
AN 91156109 MEDLINE
TI Neurochemical characterization of dopaminergic effects of **opipramol**, a potent sigma receptor **ligand**, in vivo.
AU Rao T S; Cler J A; Mick S J; Dilworth V M; Contreras P C; Iyengar S; Wood P L
CS CNS Diseases Research, G.D. Searle & Co., Monsanto Company, St Louis, Missouri 63198..
SO NEUROPHARMACOLOGY, **(1990 Dec)** 29 (12) 1191-7.
Journal code: NZB. ISSN: 0028-3908.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9106
AB Opipramol, a tricyclic antidepressant drug, potently interacted with sigma recognition sites labelled by [3H](+)-3-hydroxyphenyl)N-(1-propyl)piperidine [(3H](+)-3-PPP) with a Ki value of 50 +/- 8 nM and with minimal affinity for phencyclidine receptors (Ki greater than 30,000 nM). Opipramol potently increased the metabolism of dopamine in the striatum, olfactory tubercle and pyriform cortex of the rat and increased the release of dopamine from the striatum of the mouse, as measured by increases in the levels of 3-methoxytyramine in vivo. Opipramol increased plasma prolactin in the rat, only at a dose as large as 50 mg/kg dose. Irreversible inactivation of dopamine receptors by EEDQ (N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline) did not affect the opipramol-induced increases in levels of dihydroxyphenylacetic acid (DOPAC) in the striatum of the rat, indicating a predominant role of activation of sigma receptors in the dopaminergic effects of opipramol. However, pretreatment with the putative sigma ligand, rimcazole, markedly potentiated the ability of opipramol to increase the metabolism of release of DA in the striatum of the mouse in vivo. These results suggest that rimcazole and opipramol interact at two distinct receptors, the pharmacological significance of which is yet to be elucidated.
CT Check Tags: Animal; Male
Brain: DE, drug effects
*Brain: ME, metabolism
Corpus Striatum: ME, metabolism
*Dopamine: ME, metabolism

Haloperidol: PD, pharmacology
Homovanillic Acid: ME, metabolism
Ligands
Mice
*Opipramol: PD, pharmacology
Organ Specificity
Phencyclidine: ME, metabolism
Piperidines: ME, metabolism
Quinolines: PD, pharmacology
Rats
Rats, Inbred Strains
Receptors, Neurotransmitter: ME, metabolism
Receptors, Opioid: DE, drug effects
***Receptors, Opioid: PH, physiology**
3,4-Dihydroxyphenylacetic Acid: ME, metabolism

L17 ANSWER 30 OF 70 MEDLINE
AN 91094539 MEDLINE
TI Differential effects of cyanogen bromide on **ligand** binding by mu, delta and kappa **opioid** receptors.
AU Hiller J M; Fan L Q; Simon E J
CS Department of Psychiatry, New York University Medical Center, N.Y. 10016..
NC DA-00017 (NIDA)
SO LIFE SCIENCES, **(1990)** 47 (24) 2225-30.
Journal code: L62. ISSN: 0024-3205.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9104
AB Guinea pig brain membranes treated with cyanogen bromide (CNBr) demonstrate a loss in the number of mu opioid receptors and a lower binding affinity of delta opioid receptors. These receptor changes are irreversible. Results from ligand protection experiments support the hypothesis that the location of the methionine groups, the sites at which CNBr cleaves peptides, differs between these two types of opioid receptors. Kappa receptors are significantly less sensitive to the action of CNBr than mu or delta receptors.
CT Check Tags: Animal; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Brain: DE, drug effects
Brain: ME, metabolism
Cell Membrane: DE, drug effects
*Cyanogen Bromide: PD, pharmacology
Enkephalins: ME, metabolism
Guinea Pigs
Ligands
Methionine: ME, metabolism
Naloxone: ME, metabolism

Oligopeptides: ME, metabolism
***Receptors, Opioid: DE, drug effects**
Receptors, Opioid: ME, metabolism

L17 ANSWER 31 OF 70 MEDLINE
AN 91042966 MEDLINE
TI The bivalent **ligand** approach in the design of highly selective **opioid** receptor antagonists.
AU Portoghese P S
CS Department of Medicinal Chemistry, College of Pharmacy, University of Minnesota, Minneapolis 55455..
SO NIDA RESEARCH MONOGRAPH, **(1990)** 96 3-20. Ref: 23
Journal code: NRM. ISSN: 1046-9516.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 9102
CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
*Drug Design
Isomerism
Ligands
*Narcotic Antagonists: PD, pharmacology
***Receptors, Opioid: DE, drug effects**
Structure-Activity Relationship

L17 ANSWER 32 OF 70 MEDLINE
AN 90325227 MEDLINE
TI Electrophilic alpha-methylene-gamma-lactone and isothiocyanate **opioid ligands** related to etorphine.
AU Klein P; Nelson W L; Yao Y H; Simon E J
CS Department of Medicinal Chemistry, School of Pharmacy, University of Washington, Seattle 98195.
NC DA-03933 (NIDA)
DA-00017 (NIDA)
SO JOURNAL OF MEDICINAL CHEMISTRY, **(1990 Aug)** 33 (8) 2286-96.
Journal code: J0F. ISSN: 0022-2623.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9011
AB Isothiocyanate and alpha-methylene-gamma-lactone analogues of 6,14-endo-ethenotetrahydrothebaine and -oripavine were prepared with the electrophilic groups being located at C-19 in the C-7 alpha-side chain. Isothiocyanates were prepared in the N-Me and N-CPM (N-cyclopropylmethyl) series, both as the phenols and 3-O-methyl ethers from the diastereomeric amines formed from reductive

amination of thevinone (2) and N-(cyclopropylmethyl)northevinone (13). Although addition of the organozinc reagent from methyl alpha-bromomethacrylate to 25 failed, addition to 3-O-protected aldehydes 27 and 35 produced, after subsequent deprotection, alpha-methylene-gamma-lactones 29 and 37, respectively. In the opioid receptor displacement assays against [3H]bremazocine as the radiolabeled ligand, the phenolic compounds were most potent with N-CPM isothiocyanates 20 and 21 showing IC50s of 0.32 and 0.76 nM, respectively, and N-CPM alpha-methylene-gamma-lactone 37 having an IC50 = 1.0 nM. Compound 37 showed irreversible effects in the binding assay which were mu-selective, as demonstrated by analogous experiments using [3H]DAGO, and naloxone was found to protect against the irreversible effects. This observation suggests that a receptor-bound nucleophile is located at a position where it can readily reach the alpha-methylene group of lactone 37.

CT Check Tags: Support, U.S. Gov't, P.H.S.
Chemistry
Enkephalins: ME, metabolism
*Etorphine: AA, analogs & derivatives
Etorphine: ME, metabolism
*Lactones
Ligands
Molecular Structure
*Morphinans
Naloxone: PD, pharmacology
Nuclear Magnetic Resonance
***Receptors, Opioid: ME, metabolism**
Spectrophotometry, Infrared
Stereoisomerism
Thebaine: AA, analogs & derivatives
Thebaine: CS, chemical synthesis
Thebaine: ME, metabolism
*Thiocyanates

L17 ANSWER 33 OF 70 MEDLINE

AN 90234981 MEDLINE

TI **Opioid** receptor **ligands** in the neonatal rat spinal cord: binding and in vitro depression of the nociceptive responses.

AU James I F; Bettaney J; Perkins M N; Ketchum S B; Dray A

CS Sandoz Institute for Medical Research, London.

SO BRITISH JOURNAL OF PHARMACOLOGY, **(1990 Mar)** 99 (3) 503-8. Journal code: B00. ISSN: 0007-1188.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 9008

AB 1. Opioid receptors in the neonatal rat spinal cord have been characterized by measurements of ligand binding to crude membrane

fractions and by functional tests on the nociceptive spinal response in a spinal cord-tail preparation in vitro. 2. There were high affinity binding sites for [3H]-[D-Ala2, MePhe4, Gly(ol)5]enkephalin (DAGOL), [3H]-U69593, and [3H]-ethylketocyclazocine (EKC) on spinal cord membranes from neonatal rats. Hill slopes for binding of [3H]-DAGOL and [3H]-U69593 were close to unity. The Hill slope for binding of [3H]-EKC was less than unity, even after its interactions at mu-receptors had been blocked with 100 nM unlabelled DAGOL. Binding sites for [3H]-[D-Pen2, D-Pen5]enkephalin (DPDPE) could not be detected. 3. In competition assays U50488 was as potent as PD117302 and U69593 in competition for either [3H]-U69593 or [3H]-EKC binding sites. Hill slopes for a range of competing ligands at [3H]-DAGOL or [3H]-U69593 sites were close to unity. Hill slopes for competition at [3H]-EKC sites were less than one. 4. In the spinal cord-tail preparation from neonatal rats, opioid receptor agonists depressed spinal nociceptive responses evoked by application of capsaicin or heat to the tail. The order of potency was DAGOL greater than U69593 = PD117302 greater than morphine greater than U50488 = [D-Pen2, L-Pen5]enkephalin (DPLPE). 5. The antagonist naloxone was about equally potent against DAGOL, morphine and DPLPE, and about ten times less potent against U69593 and PD117302. The effects of U50488 were much less sensitive to blockade by naloxone than the effects of PD11703 or U69593.(ABSTRACT TRUNCATED AT 250 WORDS)

CT Check Tags: Animal; In Vitro
Animals, Newborn
Cyclazocine: AA, analogs & derivatives
Cyclazocine: ME, metabolism
Cyclazocine: PD, pharmacology
Enkephalins: ME, metabolism
Enkephalins: PD, pharmacology
Kinetics
Ligands
Morphine: PD, pharmacology
Muscle, Smooth, Vascular: DE, drug effects
Muscle, Smooth, Vascular: ME, metabolism
Naloxone: PD, pharmacology
Narcotics: PD, pharmacology
*Nociceptors: DE, drug effects
Pyrrolidines: PD, pharmacology
Rats
***Receptors, Opioid: DE, drug effects**
Receptors, Opioid: ME, metabolism
*Spinal Cord: ME, metabolism

L17 ANSWER 34 OF 70 MEDLINE
AN 90222193 MEDLINE
TI Chimeric opioid peptides: tools for identifying opioid receptor types.
AU Xie G X; Miyajima A; Yokota T; Arai K; Goldstein A

CS Department of Molecular Biology, DNAX Research Institute of Molecular and Cellular Biology, Palo Alto, CA 94304.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1990 Apr) 87 (8) 3180-4.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9007
AB We synthesized several chimeric peptides in which the N-terminal nine residues of dynorphin-32, a peptide selective for the kappa opioid receptor, were replaced by opioid peptides selective for other **opioid receptor** types. Each **chimeric** peptide retained the high affinity and type selectivity characteristic of its N-terminal sequence. The common C-terminal two-thirds of the chimeric peptides served as an epitope recognized by the same monoclonal antibody. When bound to receptors on a cell surface or membrane preparation, these peptides could still bind specifically to the monoclonal antibody. These chimeric peptides should be useful for isolating mu, delta, and kappa opioid receptors and for identifying opioid receptors on transfected cells in expression cloning procedures. The general approach using chimeric peptides should be applicable to other peptide receptors.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Amino Acid Sequence
Antibodies, Monoclonal: DU, diagnostic use
Binding, Competitive
Brain: ME, metabolism
Cell Membrane: ME, metabolism
Chimera
*Endorphins: ME, metabolism
Enzyme-Linked Immunosorbent Assay
Guinea Pigs
Kinetics
Molecular Sequence Data
***Receptors, Opioid: ME, metabolism**
Structure-Activity Relationship

L17 ANSWER 35 OF 70 MEDLINE
AN 90133778 MEDLINE
TI Conjugate addition **ligands** of **opioid** antagonists. Methacrylate esters and ethers of 6 alpha- and 6 beta-naltrexol.
AU Olsen L D; Klein P; Nelson W L; Yao Y H; Simon E J
CS Department of Medicinal Chemistry, School of Pharmacy, University of Washington, Seattle 98195..
NC DA-3933 (NIDA)
DA-0017 (NIDA)
SO JOURNAL OF MEDICINAL CHEMISTRY, **(1990 Feb)** 33 (2) 737-41.

Journal code: J0F. ISSN: 0022-2623.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9005
AB Alpha- and beta-naltrexol derived esters 9 and 10 and ethers 11 and 12, each containing the alpha, beta-unsaturated ester functionality, were prepared as conformationally more flexible analogues of spiro-alpha-methylene-gamma-lactones 5 and 6. All were active in the opioid radioreceptor binding assay against [3H]bremazocine and more active against [3H]DAGO, indicating mu-subtype selectivity, but only ether 12 showed significant irreversible activity. We conclude that small structural changes, made in very closely related electrophilic opioids, lead to changes in receptor binding. All four compounds were long-acting antagonists to morphine in mice, with ester 10 being approximately equipotent with naltrexone.
CT Check Tags: Animal; In Vitro; Support, U.S. Gov't, P.H.S.
Benzomorphans: ME, metabolism
Binding, Competitive
Cattle
Caudate Nucleus: ME, metabolism
Enkephalins: ME, metabolism
Esters
Ethers
Ligands
Methacrylates
*Naltrexone: AA, analogs & derivatives
Naltrexone: CS, chemical synthesis
Naltrexone: ME, metabolism
***Receptors, Opioid: DE, drug effects**
Structure-Activity Relationship

L17 ANSWER 36 OF 70 MEDLINE
AN 90052492 MEDLINE
TI P-8502--a new mu selective **opioid** receptor **ligand**
.
AU Ge B L; Zhang H P; Xu Y P; Zheng W J
SO CHUNG-KUO YAO LI HSUEH PAO [ACTA PHARMACOLOGICA SINICA], **(1989 Jan)** 10 (1) 13-6.
Journal code: 1P9. ISSN: 0253-9756.
CY China
DT Journal; Article; (JOURNAL ARTICLE)
LA Chinese
EM 9002
AB The analgesic potencies of 3-[beta-(p-amino)-phenethyl)-9 beta-methoxy-9 alpha-(m-methoxyphenyl)-3- azabicyclo [3,3,1] nonane (P-8502) and 3-[beta-(p-monoester fumarylamido)-phenethyl]-9 beta-methoxy-9 alpha-(m-methoxyphenyl)-3-azabicyclo [3,3,1] nonane (P-8511) were examined. The analgesic ED50 of P-8502 and P-8511 were

55 and 200 micrograms/kg (mice, ip, hot plate), and 30 and 95 micrograms/kg (rat, sc, tail flick), respectively. The duration of the analgesic action of P-8511 (about 4 h) was longer than that of P-8502 (about 1.5 h, rat, sc, tail flick). Binding assay showed that P-8502 had a high ratio of delta/mu, kappa/mu: IC50 (DPDPE)/IC50 (DAGO) = 399; IC50(DAD-LE)/IC50 (DAGO) = 1498; IC50 (kappa)/IC50 (DAGO) = 159. In conclusion, P-8502 appears to be a new mu selective opioid receptor ligand, whereas P-8511 has no such selectivity.

CT Check Tags: Animal; Female; Male
*Analgesics
*Bicyclo Compounds: PD, pharmacology
Binding, Competitive
*Bridged Compounds: PD, pharmacology
English Abstract
Ligands
Mice
*Pain: PP, physiopathology
Rats
Receptors, Opioid: CL, classification
Sensory Thresholds: DE, drug effects

L17 ANSWER 37 OF 70 MEDLINE
AN 89355528 MEDLINE
TI **Opiate** receptors: **ligands** and methods of study.
AU Olley J E
CS Department of Pharmacology, Faculty of Medicine, Monash University, Clayton, Victoria, Australia..
SO CLINICAL AND EXPERIMENTAL PHARMACOLOGY AND PHYSIOLOGY, **(1989 Jun)** 16 (6) 535-8. Ref: 21
Journal code: DD8. ISSN: 0305-1870.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 8912
AB 1. An introduction to the current knowledge of the mu-, kappa- and delta-opioid receptors will be given. 2. The many problems associated with opiate ligands with respect to selectivity, potency, slow receptor kinetics, instability and poor access to the central nervous system will be discussed. 3. Current systems for analysis of the receptor profile of opiate ligand activity will be given. 4. The properties of opioid ligands will be discussed in the context of the identified problems.
CT Check Tags: Animal; Human
Ligands
***Receptors, Opioid: DE, drug effects**

L17 ANSWER 38 OF 70 MEDLINE

AN 89100752 MEDLINE
TI An endogenous **ligand** for the sigma **opioid** binding site.
AU Contreras P C; DiMaggio D A; O'Donohue T L
CS Experimental Therapeutics Branch, National Institute of Neurological and Communicative Disorders and Stroke, Bethesda, Maryland 20892.
NC 1F34GM10089-01A1 (NIGMS)
SO SYNAPSE, **(1987)** 1 (1) 57-61.
Journal code: VFL. ISSN: 0887-4476.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8904
AB It had been suggested that phencyclidine (PCP) and sigma opioids exert their similar psychotomimetic effects through a common receptor. Recently, however, there have been several reports demonstrating significant differences between the binding of PCP and SKF 10,047, a sigma opioid agonist, which suggests that there may be distinct PCP and sigma opioid receptors. If these differences in binding represent different receptors, then there may be different endogenous ligands for each receptor. Using porcine brains, which have already been used to isolate and purify an endogenous ligand for the PCP receptor, another factor has been isolated that inhibited the binding of [3H]-(+)SKF 10,047 and not the binding of [3H]-PCP. This factor appears to be a peptide or protein because incubation of the active fraction with pronase, a nonspecific peptidase, eliminated the ability of the porcine fractions to inhibit the binding of [3H]-(+)SKF 10,047. These findings suggest the existence of an endogenous ligand for sigma opioid receptors, which is different from the previously identified endogenous ligand for PCP receptors.
CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
*Brain: ME, metabolism
*Endorphins: ME, metabolism
Kinetics
Ligands
Phenazocine: AA, analogs & derivatives
Phenazocine: ME, metabolism
Phencyclidine: ME, metabolism
Receptors, Opioid: IP, isolation & purification
***Receptors, Opioid: ME, metabolism**
Swine

L17 ANSWER 39 OF 70 MEDLINE
AN 89017125 MEDLINE
TI Pharmacological study on irreversible ligands of opiate receptors. I. alpha-CAO as agonist of irreversible ligand of opiate receptors.
AU Li L Y; Li M X; Ye C Y; Suo C L; Jin Y C; Chou Z B; Liu M Q; Zhu C L
SO PROCEEDINGS OF THE CHINESE ACADEMY OF MEDICAL SCIENCES AND THE

PEKING UNION MEDICAL COLLEGE, (1988) 3 (1) 20-5.
Journal code: PSU. ISSN: 0258-8757.
CY China
DT Journal; Article; (JOURNAL ARTICLE)
LA English
EM 8901
CT Check Tags: Animal
Guinea Pigs
***Ligands**
Mice
Rats
***Receptors, Opioid: DE, drug effects**
*Thebaine: AA, analogs & derivatives
Thebaine: PD, pharmacology

L17 ANSWER 40 OF 70 MEDLINE
AN 89014352 MEDLINE
TI Photoaffinity labeling of **opioid** delta receptors with an iodinated azido-**ligand**: [125I][D-Thr2,pN3Phe4,Leu5]enkephalyl-Thr6.
AU Bochet P; Icard-Liepkalns C; Pasquini F; Garbay-Jaureguiberry C; Beaudet A; Roques B; Rossier J
CS Laboratoire de Physiologie Nerveuse, CNRS, Gif-sur-Yvette, France..
SO MOLECULAR PHARMACOLOGY, **(1988 Oct)** 34 (4) 436-43.
Journal code: NGR. ISSN: 0026-895X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8901
AB The photoaffinity ligand of the delta opioid receptor Tyr-D-Thr-Gly-pN3Phe-Leu-Thr (azido-DTLET) was iodinated and purified by high performance liquid chromatography. Monoiodo-azido-DTLET displayed a high affinity (KD = 15 nM) and is selective (Kl mu/Kl delta = 9.8) for rat brain delta opioid receptors (for comparison, the corresponding values for tritiated azido-DTLET are KD = 1.66 nM and Kl mu/Kl delta = 27). On rat brain sections, the anatomical distribution of [125I]azido-DTLET binding sites revealed by autoradiography corresponds to that of delta receptors. On rat brain membrane homogenates and NG108-15 hybrid cells, UV irradiation of the receptor-ligand complex results in the irreversible binding to membrane proteins of 14% of the bound radioactivity Gel electrophoresis of [125I]azido-DTLET-labeled proteins followed by autoradiography shows a different pattern in rat brain and NG108-15 cells. In rat brain, labeling of two of these proteins, with molecular weights of 44,000 and 34,000, was inhibited by 30 nmol/liter of nonradioactive DTLET, a delta-selective ligand but not by the same concentration of [D-Ala2,N-Me-Phe4,Gly5-ol]-enkephalin, a mu-selective ligand. In NG108-15 cells, this 44-kDa protein was not visualized; the main band was at 33 kDa and

disappeared in the presence of levorphanol.
CT Check Tags: Animal; In Vitro; Support, Non-U.S. Gov't
Affinity Labels
*Azides
Brain: ME, metabolism
Cell Line
Enkephalins
Ligands
Mice
*Oligopeptides
Photochemistry
Rats
***Receptors, Opioid**
Receptors, Opioid: ME, metabolism

L17 ANSWER 41 OF 70 MEDLINE
AN 88334834 MEDLINE
TI Interaction of enantiomeric pairs of **opiates** with phencyclidine binding sites in rat brain: identification of (+) pentazocine as a **ligand** potentially suitable for imaging sigma binding sites using positron emission tomography.
AU Rothman R B; Bykov V; Newman A H; Jacobson A E; Rice K C
CS Laboratory of Clinical Science, NIMH, Bethesda, MD 20892.
SO NEUROPEPTIDES, **(1988 Jul)** 12 (1) 1-5.
Journal code: NZC. ISSN: 0143-4179.
CY SCOTLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8812
AB Some unnatural opiates, which do not interact with classical opiate receptors, interact with phencyclidine (PCP) receptors. Among their many pharmacological actions, drugs which bind to the PCP receptor antagonize the actions of glutamic acid mediated via the NMDA excitatory amino acid receptor, leading to their potential use as anti-ischemic and anticonvulsant agents. Despite an enormous effort, identification of a PCP receptor antagonist, which would be useful for research and therapeutics, has not yet been reported. Chemical modification of unnatural opiates as a means to produce a PCP antagonist, or PCP agonists with properties different than PCP, has not been fully explored. Towards this end, we determined the equilibrium dissociation constants of eight enantiomeric pairs of opiates for the rat brain PCP receptor.
CT Check Tags: Animal; Male
*Brain: ME, metabolism
Ligands
*Narcotics: ME, metabolism
*Pentazocine: AN, analysis
*Phencyclidine: ME, metabolism
Rats

Rats, Inbred Strains
*Receptors, Neurotransmitter: ME, metabolism
Receptors, Opioid: ME, metabolism
Stereoisomerism
Tomography, Emission-Computed

L17 ANSWER 42 OF 70 MEDLINE
AN 88165633 MEDLINE
TI Isolation of **opiate** receptor **ligands** in coffee.
AU Wynne K N; Familari M; Boublik J H; Drummer O H; Rae I D; Funder J W
CS Ewen Downie Metabolic Unit, Alfred Hospital, Prahran, Victoria, Australia..
SO CLINICAL AND EXPERIMENTAL PHARMACOLOGY AND PHYSIOLOGY, **(1987 Oct)** 14 (10) 785-90.
Journal code: DD8. ISSN: 0305-1870.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8807
AB 1. We have reported previously that instant coffee contains ligands for opiate receptors with characteristics similar to those of opiate antagonists. 2. A concentrate of receptor-active ligands from instant coffee was prepared by serial treatments involving Amberlite XAD-2, flash chromatography and gel permeation chromatography. 3. Examination of the final concentrate by GC-MS showed the presence of a number of isomeric (iso)feruloylquinic acid lactones. 4. It is suggested that the synthesis and biological testing of each quinide isomer will establish which is responsible for the opiate receptor activity of instant coffee.
CT Check Tags: Animal; In Vitro; Male; Support, Non-U.S. Gov't
Brain Chemistry: DE, drug effects
*Coffee: AN, analysis
Ligands
Mass Fragmentography
*Narcotics: IP, isolation & purification
Narcotics: PD, pharmacology
Rats
Rats, Inbred Strains
***Receptors, Opioid: AN, analysis**

L17 ANSWER 43 OF 70 MEDLINE
AN 88035919 MEDLINE
TI Hybrid bivalent ligands with opiate and enkephalin pharmacophores.
AU Portoghese P S; Larson D L; Ronsisvalle G; Schiller P W; Nguyen T M; Lemieux C; Takemori A E
CS Department of Medicinal Chemistry, University of Minnesota, Minneapolis 55455..
SO JOURNAL OF MEDICINAL CHEMISTRY, (1987 Nov) 30 (11) 1991-4.
Journal code: J0F. ISSN: 0022-2623.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8802
AB Bivalent ligands consisting of oxymorphamine and [D-Glu2]enkephalin pharmacophores linked through a spacer attached to the 6-amino group of the former and D-Glu of the latter were synthesized in an effort to investigate the possible coexistence of mu and delta recognition sites in the same opioid receptor complex. Of the two bivalent ligands (1,2) synthesized, only 1 had substantially greater antinociceptive potency in mice than its monovalent analogues (1a, 1b). Testing of 1, 1a, and 1b in the guinea pig ileum preparation (GPI) revealed a potency profile similar to that found in vivo, whereas no correlation was observed in the mouse vas deferens (MVD). Binding data indicated the same rank-order affinities at delta receptors as the opioid activities in the GPI and in mice. However, mu binding exhibited no relationship with activity. These results are consistent with the simultaneous occupation of mu and delta by a single bivalent ligand 1, but they are also in harmony with the interaction of 1 with an opioid receptor and an accessory binding site.
CT Check Tags: Animal; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Analgesics: PD, pharmacology
*Enkephalins: ME, metabolism
Enkephalins: PD, pharmacology
Guinea Pigs
*Hydromorphone: AA, analogs & derivatives
***Ligands**
Mice
Muscle, Smooth: DE, drug effects
Naloxone: PD, pharmacology
*Oxymorphone: AA, analogs & derivatives
Oxymorphone: PD, pharmacology
***Receptors, Opioid: ME, metabolism**

L17 ANSWER 44 OF 70 MEDLINE
AN 87273690 MEDLINE
TI Pharmacological study on an irreversible **ligand** of **opioid** receptors- 7 alpha-bis (beta-chloroethyl) amino-6, 14-endoetheno-tetrahydrooripavine (alpha-CAO).
AU Li L Y; Li M X; Ye C Y; Suo C L; Jin Y C; Qiu Z B; Liu M Q; Zhu C L
SO CHUNG-KUO I HSUEH KO HSUEH YUAN HSUEH PAO ACTA ACADEMIAE MEDICINAE SINICAE, **(1987 Apr)** 9 (2) 118-24.
Journal code: CZS. ISSN: 1000-503X.
CY China
DT Journal; Article; (JOURNAL ARTICLE)
LA Chinese

EM 8711
CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
Analgesics
*Analgesics, Opioid: PD, pharmacology
Binding Sites
English Abstract
Guinea Pigs
Ligands
Mice
*Muscle Contraction: DE, drug effects
Rabbits
Rats
***Receptors, Opioid**
Receptors, Opioid: DE, drug effects
Receptors, Opioid: ME, metabolism
*Thebaine: AA, analogs & derivatives
Thebaine: PD, pharmacology

L17 ANSWER 45 OF 70 MEDLINE
AN 87080548 MEDLINE
TI Ontogenesis of delta-**opioid** receptors in rat brain using [3H][D-Pen2,D-Pen5]enkephalin as a binding **ligand**.
AU McDowell J; Kitchen I
SO EUROPEAN JOURNAL OF PHARMACOLOGY, **(1986 Sep 9)** 128 (3) 287-9.
Journal code: EN6. ISSN: 0014-2999.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8704
AB The ontogenesis of delta-opioid receptors has been studied in the postnatal period up to day 50 using the highly selective delta-site ligand [3H][D-Pen2,D-Pen5]enkephalin ([3H]DPDPE) in binding studies. Analyses of saturation curves revealed marked increases in binding capacities between the second and fourth postnatal week with little change in affinity. In contrast to findings with [3H][D-Ala2,D-Leu5]enkephalin binding could not be detected before postnatal day 10 which may be associated with the low affinity and specific activity of DPDPE. A low specific binding for [3H]DPDPE poses methodological problems in the use of this ligand for ontogenic studies.
CT Check Tags: Animal; Female; Male; Support, Non-U.S. Gov't
*Brain: GD, growth & development
Brain: ME, metabolism
*Enkephalins: PD, pharmacology
Kinetics
Ligands
Rats
Rats, Inbred Strains

***Receptors, Opioid: ME, metabolism**

L17 ANSWER 46 OF 70 MEDLINE
AN 87041536 MEDLINE
TI 1,3-Di(2-[5-3H]tolyl)guanidine: a selective **ligand** that labels sigma-type receptors for psychotomimetic **opiates** and antipsychotic drugs.
AU Weber E; Sonders M; Quarum M; McLean S; Pou S; Keana J F
NC MH40303 (NIMH)
GM27137 (NIGMS)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1986 Nov)** 83 (22) 8784-8.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8702
AB Brain sigma-type receptors are thought to mediate hallucinogenic effects of certain benzomorphan opiates in humans. The biochemical characterization of sigma receptors has been difficult because of the lack of potent and selective ligands. We report here the synthesis and characterization of a tritiated, symmetrically substituted guanidine derivative, 1,3-di(2-[5-3H]tolyl)guanidine ([3H]Tol2Gdn), that binds with high affinity to a single population of binding sites in guinea pig brain membrane preparations. The [3H]Tol2Gdn binding site displays stereoselectivity for dextrorotatory optical isomers of benzomorphan opiates known to have sigma-type behavioral effects. Furthermore, the [3H]Tol2Gdn binding site has a high affinity for haloperidol and for phenothiazine antipsychotics, which have antihallucinatory properties in humans. The drug-selectivity profile of [3H]Tol2Gdn binding closely correlates with the drug-selectivity profile of tritiated (+)-3-(3-hydroxyphenyl)-N-(1-propyl)piperidine [+)-[3H]3-PPP) binding to guinea pig brain membrane receptors. (+)-[3H]3-PPP has been proposed to be a selective sigma-receptor ligand [Largent, B. L., Gundlach, A. L. & Snyder, S. H. (1984) Proc. Natl. Acad. Sci. USA 82, 4983-4987]. Receptor autoradiography using [3H]Tol2Gdn on slide-mounted rat and guinea pig brain sections reveals a heterogeneous distribution pattern of enriched binding in limbic and sensorimotor structures of the brain. These results indicate that [3H]Tol2Gdn is a selective ligand for the sigma-site. Availability of this sigma-receptor probe should greatly facilitate the physiological, biochemical, and pharmacological characterization of sigma receptors in brain.
CT Check Tags: Animal; In Vitro; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Antipsychotic Agents: PD, pharmacology
*Benzomorphans: PD, pharmacology
Binding Sites

Brain: ME, metabolism
*Guanidines: ME, metabolism
Guinea Pigs
*Hallucinogens: PD, pharmacology
Ligands
*Morphinans: PD, pharmacology
Piperidines: ME, metabolism
Rats
Rats, Inbred Strains
Receptors, Neurotransmitter: AN, analysis
Receptors, Opioid: AN, analysis
***Receptors, Opioid: ME, metabolism**
Tritium: DU, diagnostic use

L17 ANSWER 47 OF 70 MEDLINE
AN 86238407 MEDLINE
TI Irreversible ligands of opioid receptors and their use in the study of these receptors.
AU Li M X; Jin Y C
SO YAO HSUEH HSUEH PAO [ACTA PHARMACEUTICA SINICA], (1985 Dec) 20 (12) 940. Ref: 66
Journal code: 1PU. ISSN: 0513-4870.
CY China
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA Chinese
EM 8609
CT ***Ligands**
***Receptors, Opioid**
Receptors, Opioid: IP, isolation & purification

L17 ANSWER 48 OF 70 MEDLINE
AN 86077079 MEDLINE
TI [Specific binding of N-allylnormetazocine (SKF 10047), a **ligand** of sigma-**opioid** receptors, with liver membranes].
Spetsificheskoe sviazyvanie **liganda** sigma-**opioidnykh** retseptorov--N-allilnormetazotsina (SKF 10047)--s membranami pecheni.
AU Samovilova N N; Iarygin K N; Vinogradov V A
SO BIOORGANICHESKAIA KHIMIIA, **(1985 Oct)** 11 (10) 1380-4.
Journal code: 9Z8. ISSN: 0132-3423.
CY USSR
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
FS Priority Journals
EM 8603
AB A sigma-opioid receptor ligand, N-allylnormetazocine (SKF 10047), binds specifically and reversibly to rat liver membranes. The rat liver binding sites for SKF 10047 are similar to sigma-opioid CNS

receptors. They fail to interact with classical opiates (morphine, naloxone) and opioid peptides but bind with high affinity benzomorphans (bremazocine, SKF 10047) and various psychotropic drugs (haloperidol, imipramine, phencyclidine etc).
CT Check Tags: Animal; Comparative Study; Human; In Vitro; Male
*Brain: ME, metabolism
English Abstract
Guinea Pigs
Kinetics
Ligands
*Liver: ME, metabolism
Membranes: ME, metabolism
Mice
Mice, Inbred BALB C
*Phenazocine: AA, analogs & derivatives
Phenazocine: ME, metabolism
Rats
Rats, Inbred Strains
Receptors, Opioid: DE, drug effects
***Receptors, Opioid: ME, metabolism**
Species Specificity

L17 ANSWER 49 OF 70 MEDLINE
AN 86062567 MEDLINE
TI Hybromet: a **ligand** for purifying **opioid** receptors.
AU Archer S; Michael J; Osei-Gyimah P; Seyed-Mozaffari A; Zukin R S; Maneckjee R; Simon E J; Gioannini T L
SO JOURNAL OF MEDICINAL CHEMISTRY, **(1985 Dec)** 28 (12) 1950-3. Journal code: J0F. ISSN: 0022-2623.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8603
AB Condensation of the Grignard reagent derive from 2-[4-(allyloxy)phenyl]ethyl bromide (4b) with 7 alpha-acetyl-6,14-endo-ethenotetrahydrothebaine (5) furnished the (R) tertiary carbinol, 7, which upon methoxymercuration followed by treatment with the KBr gave the bromomercurio compound 10 (Hybromet). The corresponding N-cyclopropylmethyl analogue, 11, was prepared also. The bromomercurio compound, 1, and the mercaptobenzothiazole derivative, 3, gave allyl phenyl ether when treated with BAL at room temperature. Similar treatment of 10 with BAL gave 7 in high yield. Binding studies using rat brain homogenates indicated that 7, 13, and 14 have moderately high affinities for mu rather than delta binding sites. Although much weaker, 10 showed preferential mu binding also. These results along with the fact that 10 reacted smoothly with sulfhydryl groups suggest that Hybromet would be a suitable ligand for use in affinity chromatography.

CT Check Tags: Animal; Comparative Study; Support, U.S. Gov't, P.H.S.
Binding Sites
Brain: ME, metabolism
Chemistry
Chromatography, Affinity
Indicators and Reagents
Ligands
Naltrexone: ME, metabolism
Organomercury Compounds: CS, chemical synthesis
*Organomercury Compounds: ME, metabolism
Rats
***Receptors, Opioid: IP, isolation & purification**
Receptors, Opioid: ME, metabolism
*Thebaine: AA, analogs & derivatives
Thebaine: CS, chemical synthesis
Thebaine: ME, metabolism

L17 ANSWER 50 OF 70 MEDLINE
AN 85204095 MEDLINE
TI 3H]U-69593 a highly selective **ligand** for the **opioid** kappa receptor.
AU Lahti R A; Mickelson M M; McCall J M; Von Voigtlander P F
SO EUROPEAN JOURNAL OF PHARMACOLOGY, **(1985 Feb 26)** 109 (2) 281-4.
Journal code: EN6. ISSN: 0014-2999.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8509
AB The selective kappa agonist U-50488 was recently discovered and characterized. In this study, the receptor binding properties of [3H]U-69593, an analog of U-50488, were characterized. [3H]U-69593 binds with high affinity (3 nM) to membranes prepared from guinea pig, mouse and rat brain. The number of kappa binding sites comprise only 13%, 9% and 4% of the total opioid sites, respectively. The benzmorphans, dynorphin, and compounds structurally related to U-50488 have high affinity for this kappa site.
CT Check Tags: Animal; In Vitro; Male
*Analgesics: ME, metabolism
Benzomorphans: ME, metabolism
Brain: ME, metabolism
Guinea Pigs
Ligands
Mice
Naloxone: ME, metabolism
*Pyrrolidines: ME, metabolism
Rats
***Receptors, Opioid: ME, metabolism**

L17 ANSWER 51 OF 70 MEDLINE
AN 85135491 MEDLINE
TI Two new **opioid** delta-receptor **ligands**: a highly selective agonist and a potent selective antagonist in in vitro isolated preparations.
AU Ueki M; Aoki K; Kajiwara M; Shinozaki K; Inoue H; Oka T
SO JAPANESE JOURNAL OF PHARMACOLOGY, **(1984 Dec)** 36 (4) 485-9. Journal code: KO7. ISSN: 0021-5198.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8506

AB N,N-Diallyl derivatives of enkephalin analogues were chemically synthesized, and their biological activities were estimated in vitro isolated preparations. N,N-Diallyl-[D-Ala2, D-Leu5]-enkephalin [test compound I] at doses up to 10 microM did not inhibit the electrically-evoked contractions of guinea-pig ileum, which had been suggested to contain opioid mu- and kappa-receptors, but it significantly depressed the contractions of mouse vas deferens, which had been indicated to contain mu-, kappa- and delta-receptors, suggesting that test compound I did not act on both mu- and kappa-receptors, but acted on delta-receptors. Additionally, the Ke (equilibrium dissociation constant) values against test compound I of naloxone were approximately 30 nM and similar to those of Mr 2266, also indicating that test compound I acted as a delta agonist. Moreover, the Ke values of ICI 154129 against compound I were approximately 340 nM, strongly suggesting that test compound I acted as a delta agonist. The Ke values of bis-[N,N-diallyl-[D-Ala2, Leu5]-enkephalyl]-cystine [test compound II] against [D-Ala2, D-Leu5]-enkephalin in mouse vas deferens and morphine or ethylketocyclazocine in guinea-pig ileum were 44.9 nM and 5.00 or 11.3 microM, respectively, showing that test compound II was a potent selective opioid delta antagonist. In conclusion, among compounds synthesized, two new opioid delta-receptor ligands, one being a highly selective agonist and the other being a potent selective antagonist in in vitro isolated preparations, were found in the present study.

CT Check Tags: Animal; In Vitro; Male
Benzomorphans: PD, pharmacology
*Enkephalin, Leucine: AA, analogs & derivatives
Enkephalin, Leucine: PD, pharmacology
Enkephalins: PD, pharmacology
Guinea Pigs
Ileum: DE, drug effects
Kinetics
Ligands
Mice
Mice, Inbred ICR
Muscle Contraction: DE, drug effects

*Muscle, Smooth: DE, drug effects
Naloxone: PD, pharmacology
Narcotic Antagonists: PD, pharmacology
***Receptors, Opioid: ME, metabolism**
Vas Deferens: DE, drug effects

L17 ANSWER 52 OF 70 MEDLINE
AN 85127208 MEDLINE
TI Interaction of dopamine receptor ligands with subtypes of the opiate receptor.
AU Boublik J H; Funder J W
SO EUROPEAN JOURNAL OF PHARMACOLOGY, (1984 Dec 15) 107 (1) 11-6.
Journal code: EN6. ISSN: 0014-2999.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8506
AB There are currently several studies in which individual dopamine receptor ligands have been reported to bind with relatively low affinity to opiate receptors. To extend these studies, and to examine the opiate receptor subclass selectivity of such agents, we have examined the ability of six dopamine receptor ligands (prochlorperazine, chlorpromazine, haloperidol, bromocriptine, pimozide and metoclopramide) to compete with four tritiated tracers - [3H]naloxone, [3H][D-Ala2,D-Leu5]enkephalin, [3H]morphine and [3H]ethylketocyclazocine - for binding to rat brain membrane opiate receptors. The dopamine receptor ligands displaced the labelled opiates in a dose-dependent manner, with ED50 values of 3 microM to 3 mM. Pimozide was consistently the most potent (ED50 3-14 microM), and metoclopramide the least potent (ED50 35 microM to 3.5 mM). Dopamine receptor agonists and antagonists thus interact with opiate receptors with no clear subclass selectivity, and with similar hierarchies of inhibitory potency in each of the various opiate receptor systems.
CT Check Tags: Animal; In Vitro; Male; Support, Non-U.S. Gov't
Binding, Competitive: DE, drug effects
*Brain: ME, metabolism
Bromocriptine: ME, metabolism
Bromocriptine: PD, pharmacology
Dopamine: AI, antagonists & inhibitors
Drug Interactions
Haloperidol: ME, metabolism
Haloperidol: PD, pharmacology
***Ligands**
Membranes: ME, metabolism
Metoclopramide: ME, metabolism
Metoclopramide: PD, pharmacology
Naloxone: AI, antagonists & inhibitors
Naloxone: ME, metabolism

Pimozide: ME, metabolism
Pimozide: PD, pharmacology
Prochlorperazine: ME, metabolism
Prochlorperazine: PD, pharmacology
Radioligand Assay
Rats
Rats, Inbred Strains
*Receptors, Dopamine: ME, metabolism
***Receptors, Opioid: ME, metabolism**
Tritium

L17 ANSWER 53 OF 70 MEDLINE
AN 85057948 MEDLINE
TI Probes for narcotic receptor mediated phenomena. 7. Synthesis and pharmacological properties of irreversible ligands specific for mu or delta opiate receptors.
AU Burke T R Jr; Bajwa B S; Jacobson A E; Rice K C; Streaty R A; Klee W A
SO JOURNAL OF MEDICINAL CHEMISTRY, (1984 Dec) 27 (12) 1570-4. Journal code: J0F. ISSN: 0022-2623.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8503
AB Syntheses of affinity reagents for opiate receptors based on the fentanyl, endo-ethenotetrahydrooripavine, and etonitazene carbon-nitrogen skeletons are described. The isothiocyanate, bromoacetamido, and methylfumaramido alkylating functions were employed in these compounds, some of which had previously been shown to be mu specific (12, BIT) and delta specific (8, FIT and 19, FAO) in vitro. Antinociceptive activity of the title compounds was determined in the mouse hot-plate test, which revealed that certain compounds in each class showed morphine-like activity. The binding EC50 values against [3H]Dalamid for opiate receptors in NG108-15 (delta receptors) and rat brain membranes (mu + delta receptors) are also reported. With this type of experiment, it was possible to independently measure the apparent affinity of the etonitazene congeners 12-14 for the mu and delta receptors.
CT Check Tags: Animal; Comparative Study
Benzimidazoles: AA, analogs & derivatives
Benzimidazoles: ME, metabolism
Benzimidazoles: PD, pharmacology
Cell Line
Cell Membrane: ME, metabolism
Chemistry
Drug Screening
Fentanyl: AA, analogs & derivatives
Fentanyl: ME, metabolism
Fentanyl: PD, pharmacology

Glioma: ME, metabolism
Hybrid Cells: ME, metabolism
Indicators and Reagents
*Ligands: ME, metabolism
Ligands: PD, pharmacology
Mice
*Narcotic Antagonists: CS, chemical synthesis
Neuroblastoma: ME, metabolism
Nuclear Magnetic Resonance
Rats
Receptors, Opioid: DE, drug effects
*Receptors, Opioid: ME, metabolism
Spectrum Analysis, Mass
Structure-Activity Relationship
Thebaine: AA, analogs & derivatives
Thebaine: ME, metabolism
Thebaine: PD, pharmacology

L17 ANSWER 54 OF 70 MEDLINE
AN 84031271 MEDLINE
TI Selective **ligands** for **opioid** receptors.
beta-Cyclopropylalanyl containing analogs of enkephalin.
AU Muthukumaraswamy N; Day A R; Pinon D; Liao C S; Freer R J
NC HL-19653 (NHLBI)
HL-25383 (NHLBI)
SO INTERNATIONAL JOURNAL OF PEPTIDE AND PROTEIN RESEARCH, **(1983 Sep)** 22 (3) 305-12.
Journal code: GSD. ISSN: 0367-8377.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8402
CT Check Tags: Animal; Comparative Study; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Biological Assay
*Enkephalins: CS, chemical synthesis
Enkephalins: ME, metabolism
Enkephalins: PD, pharmacology
Guinea Pigs
Ileum: DE, drug effects
Indicators and Reagents
Ligands
Muscle Contraction: DE, drug effects
Rats
*Receptors, Opioid: ME, metabolism
Structure-Activity Relationship
Vas Deferens: DE, drug effects

L17 ANSWER 55 OF 70 MEDLINE
AN 83171383 MEDLINE
TI Irreversible **ligands** with high selectivity toward delta and mu **opiate** receptors.
AU Rice K C; Jacobson A E; Burke T R Jr; Bajwa B S; Streaty R A; Klee W A
SO SCIENCE, **(1983 Apr 15)** 220 (4594) 314-6.
Journal code: UJ7. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8307
AB Alkylating agents that display strong selectivity for opiate receptor types delta or mu were prepared by appropriate modification of the structures of the strong analgesics fentanyl, etonitazene, and endoethenotetrahydrooripavine. The availability of these substances should facilitate studies of the structural basis of receptor specificity and of the physiologic roles of these receptors.
CT Check Tags: Animal
Alkylation
Benzimidazoles: AA, analogs & derivatives
Benzimidazoles: ME, metabolism
Brain: PH, physiology
Cells, Cultured
Chemistry
Enkephalin, Methionine: AA, analogs & derivatives
Enkephalin, Methionine: ME, metabolism
Fentanyl: AA, analogs & derivatives
Fentanyl: ME, metabolism
Ligands
Rats
***Receptors, Opioid: ME, metabolism**
Receptors, Opioid: PH, physiology
Thebaine: AA, analogs & derivatives
Thebaine: PD, pharmacology

L17 ANSWER 56 OF 70 MEDLINE
AN 83132216 MEDLINE
TI [Tropane **ligands** of different types of **opiate** receptors].
Tropanovye **ligandy opiatnykh** retseptorov raznogo tipa.
AU Zakusov V V; Iasnetsov V V
SO FARMAKOLOGIIA I TOKSIKOLOGIIA, **(1983 Jan-Feb)** 46 (1) 5-8.
Journal code: ETR. ISSN: 0014-8318.
CY USSR
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian

FS Priority Journals
EM 8306
AB Interaction of tropane derivatives (motropin, atropine, cocaine) with opiates (morphine) and opioids (an enkephalin amide analog) was studied according to varying tests: pain sensitivity, impulse summation in the central nervous system, respiration. It appeared that motropin is a morphine antagonist and enkephalin amide analog from the standpoint of effect on analgetic action and impulse summation, but is not their antagonist as regards the effect on respiration. Atropine is a weak morphine antagonist in terms of the effect on analgesia, impulse summation and respiration as well. Cocaine is a morphine synergist as regards all the tests indicated. Therefore, the effect of tropane derivatives on pain sensitivity, impulse summation and respiration is mediated via different opiate receptors, which does not exclude the involvement of other neurochemical mechanisms in their action.
CT Check Tags: Animal
Central Nervous System: DE, drug effects
Electric Stimulation
Endorphins: AI, antagonists & inhibitors
English Abstract
Ligands
Mice
Narcotic Antagonists: PD, pharmacology
Pain: PP, physiopathology
Rabbits
Rats
***Receptors, Opioid: PD, pharmacology**
*Tropanes: PD, pharmacology
Vocalization, Animal: DE, drug effects

L17 ANSWER 57 OF 70 MEDLINE
AN 83114186 MEDLINE
TI Photolabile ligands for opiate receptors.
AU Zioudrou C; Varoucha D; Loukas S; Streaty R A; Klee W A
SO LIFE SCIENCES, (1982 Oct 18-25) 31 (16-17) 1671-4.
Journal code: L62. ISSN: 0024-3205.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8305
AB The 2-nitro-4-azidophenyl(NAP)-D-Ala2-Leu5-Enkephalin derivatives: Try-D-Ala-Gly-Phe-Leu CONCH2CH2NH-NAP (E-NAP-EDA) and Try-D-Ala-Gly-Phe-Leu CONCH2CH2NH-COCH2CH2NHNAP(E-NAP- -Ala-EDA) were synthesized by conventional peptide methods. Their structure was determined by amino acid analysis, ultra violet, visible and infra red spectroscopy. Both peptides were shown a) to bind with high affinity to the opiate receptors of rat brain membranes and b) to inhibit strongly the contractions of electrically stimulated vas

deferens and the adenyl cyclase of the NG 108-15 cell membranes. These effects were reversed by the antagonist naloxone. Photoloysis of the rat brain membranes-(E-NAP- -Ala-EDA) complex caused a 20-30% inactivation of the opiate receptors. Inactivation was prevented when the complex was irradiated in the presence of naloxone. The radio-labeled derivatives of these enkephalin analogs may prove useful photochemical labels of the opiate receptor.

CT Check Tags: Animal
Brain: ME, metabolism
Endorphins: ME, metabolism
Enkephalin, Leucine: AA, analogs & derivatives
***Ligands: CS, chemical synthesis**
Ligands: DU, diagnostic use
Photolysis
Rats
***Receptors, Opioid: ME, metabolism**

L17 ANSWER 58 OF 70 MEDLINE
AN 83061694 MEDLINE
TI Opioid agonist and antagonist bivalent ligands as receptor probes.
AU Portoghese P S; Ronsisvalle G; Larson D L; Yim C B; Sayre L M; Takemori A E
NC DA 02659 (NIDA)
SO LIFE SCIENCES, (1982 Sep 20-27) 31 (12-13) 1283-6.
Journal code: L62. ISSN: 0024-3205.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8303
AB Bivalent ligands are molecules which contain two pharmacophores linked by a connecting chain (spanner). The present report describes the use of oxymorphamine (Oxy) and naltrexamine (Nal) as the opioid agonist and antagonist pharmacophores separated by a variable length spanner composed of succinyl-bis-oligoglycine. The agonist series, [CH2CO(Gly)nOxy]2, and antagonist series, [CH2CO(Gly)nNal]2, were synthesized (n = 0-4) and tested on the electrically stimulated GPI. All of the antagonist bivalent ligands (Nal) antagonized the effects of morphine, with the greatest potency enhancement (60 x) residing with the succinyl (n = 0) congener. A dramatically different SAR profile was observed in the agonist (Oxy) series where the greatest potency enhancement (17 x) occurs when n = 2. By contrast with the antagonist series the agonist bivalent ligand with n = 0 is equipotent to its monovalent agonist analogue. The significance of these results with respect to the possibility of discrete opioid agonist and antagonist recognition sites are discussed.
CT Check Tags: Animal; In Vitro; Support, U.S. Gov't, P.H.S.
Guinea Pigs
***Ligands**
Naltrexone: AA, analogs & derivatives

Naltrexone: PD, pharmacology
*Narcotic Antagonists: PD, pharmacology
Oxymorphone: AA, analogs & derivatives
Oxymorphone: PD, pharmacology
***Receptors, Opioid: DE, drug effects**
Structure-Activity Relationship

L17 ANSWER 59 OF 70 MEDLINE
AN 82272365 MEDLINE
TI Dynorphin and dynorphin are **ligands** for the kappa-subtype of **opiate** receptor.
AU Corbett A D; Paterson S J; McKnight A T; Magnan J; Kosterlitz H W
NC DA 00662 (NIDA)
SO NATURE, **(1982 Sep 2)** 299 (5878) 79-81.
Journal code: NSC. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8212
CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Biological Assay
Brain: ME, metabolism
*Endorphins: ME, metabolism
Enkephalins: ME, metabolism
Guinea Pigs
Ligands
Mice
Peptide Fragments: ME, metabolism
Rabbits
Radioligand Assay
Rats
Receptors, Opioid: CL, classification
***Receptors, Opioid: ME, metabolism**
Structure-Activity Relationship

L17 ANSWER 60 OF 70 MEDLINE
AN 82129119 MEDLINE
TI Dynorphin is a specific endogenous **ligand** of the kappa **opioid** receptor.
AU Chavkin C; James I F; Goldstein A
NC DA-1199 (NIDA)
DA-7063 (NIDA)
SO SCIENCE, **(1982 Jan 22)** 215 (4531) 413-5.
Journal code: UJ7. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals
EM 8206
AB In the guinea pig ileum myenteric plexus--longitudinal muscle preparation, dynorphin-(1--13) and the prototypical kappa agonist ethylketocyclazocine had equally poor sensitivity to naloxone antagonism and showed selective cross protection in receptor inactivation experiments with the alkylating antagonist beta-chlornaltrexamine. In binding assays with membranes from guinea pig brain, ethylketocyclazocine and dynorphin-(1--13) amide were more potent in displacing tritium-labeled ethylketocyclazocine than in displacing typical mu and delta opioid receptor ligands. In the two preparations studied, the dynorphin receptor appears to be the same as the kappa opioid receptor.
CT Check Tags: Animal; In Vitro; Support, U.S. Gov't, P.H.S.
Analgesics, Opioid: ME, metabolism
Binding, Competitive
Brain: ME, metabolism
Cyclazocine: AA, analogs & derivatives
Cyclazocine: ME, metabolism
*Endorphins: ME, metabolism
Enkephalins: ME, metabolism
Guinea Pigs
Ligands
Morphine Derivatives: ME, metabolism
Myenteric Plexus: ME, metabolism
Naloxone: ME, metabolism
*Peptide Fragments: ME, metabolism
***Receptors, Opioid: ME, metabolism**

L17 ANSWER 61 OF 70 MEDLINE
AN 82108185 MEDLINE
TI Assay of endogenous **opiate** receptor **ligands** in human CSF and plasma.
AU Naber D; Pickar D; Dionne R A; Bowie D L; Ewels B A; Moody T W; Soble M G; Pert C B
SO SUBSTANCE AND ALCOHOL ACTIONS/MISUSE, **(1980)** 1 (1) 83-91. Journal code: VAC. ISSN: 0191-8877.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8205
CT Check Tags: Animal; Human; Male; Support, Non-U.S. Gov't
Chromatography, Gel
Endorphins: ME, metabolism
Ligands
Radioligand Assay
Rats
Rats, Inbred Strains
***Receptors, Opioid: AN, analysis**

L17 ANSWER 62 OF 70 MEDLINE
AN 82010511 MEDLINE
TI Allylprodine analogues as receptor probes. Evidence that phenolic and nonphenolic **ligands** interact with different subsites on identical **opioid** receptors.
AU Portoghese P S; Alreja B D; Larson D L
NC DA 02220 (NIDA)
SO JOURNAL OF MEDICINAL CHEMISTRY, **(1981 Jul)** 24 (7) 782-7. Journal code: J0F. ISSN: 0022-2623.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8201
AB The m-hydroxy analogues of allylprodine and related structures have been synthesized and tested for narcotic agonist and antagonist activity on the electrically stimulated guinea pig ileum and by the hot-plate procedure in mice. It has been found that m-hydroxyallylprodine (alpha-2) is neither an agonist nor antagonist. Other phenolic congeners similarly have little or no activity. The fact that these results are in dramatic contrast with the structure-activity profile of morphine and closely related opiates has led to the proposal that the interaction of morphine and allylprodine (alpha-1) with the mu opioid receptor differs. This difference is postulated to arise from the recognition of the aromatic groups of morphine and alpha-1 by different aromatic-binding subsites of the receptor. These subsites are suggested to be identical with those which recognize the aromatic rings of the Tyr1 and Phe4 of the enkephalins and endorphins. A receptor model consistent with these results is proposed.
CT Check Tags: Animal; In Vitro; Support, U.S. Gov't, P.H.S.
Chemistry, Physical
Guinea Pigs
Ileum: DE, drug effects
Ligands
Mice
Morphine: AI, antagonists & inhibitors
Muscle Contraction: DE, drug effects
Muscle, Smooth: DE, drug effects
Narcotic Antagonists
Phenols: PD, pharmacology
*Piperidines: CS, chemical synthesis
Reaction Time: DE, drug effects
***Receptors, Opioid: DE, drug effects**
Structure-Activity Relationship

L17 ANSWER 63 OF 70 MEDLINE
AN 81024313 MEDLINE
TI D-Tyr--Ser-Gly--Phe--Leu--Thr, a highly preferential **ligand**

for delta-**opiate** receptors.
AU Gacel G; Fournie-Zaluski M C; Roques B P
SO FEBS LETTERS, **(1980 Sep 8)** 118 (2) 245-7.
Journal code: EUH. ISSN: 0014-5793.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8102
CT Check Tags: Animal; Support, Non-U.S. Gov't
Biological Assay
Guinea Pigs
Ileum: DE, drug effects
Ligands
Mice
Muscle Contraction: DE, drug effects
Oligopeptides: CS, chemical synthesis
*Oligopeptides: ME, metabolism
Oligopeptides: PD, pharmacology
***Receptors, Opioid: ME, metabolism**
Structure-Activity Relationship

L17 ANSWER 64 OF 70 MEDLINE
AN 79231629 MEDLINE
TI [Endorphines--the endogenous **ligands** of **opiate** receptors (author's transl)].
Endorphine--die endogenen **Liganden** der **Opiatrezeptoren**.
AU Teschemacher H
SO ARZNEIMITTEL-FORSCHUNG, **(1978)** 28 (8) 1268-70.
Journal code: 91U. ISSN: 0004-4172.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA German
FS Priority Journals
EM 7911
AB The demonstration of opiate receptors in the nervous tissue of vertebrates in 1973 was the starting point of an intensive search for the endogenous ligands of these receptors. During the following years, several of such "edogenous opiates", called "endorphines", were isolated from various tissues of the mammalian organism. These are peptides which are able to elicit the same effects as do opiates. Possibly, they play a role in the reaction of the organism to stress.
CT Check Tags: Animal
Amino Acid Sequence
Chemistry
*Endorphins: ME, metabolism
English Abstract
Hormones

Ligands
Neurotransmitters
***Receptors, Opioid: ME, metabolism**

L17 ANSWER 65 OF 70 MEDLINE
AN 79124197 MEDLINE
TI Unsulfated C-terminal 7-peptide of cholecystokinin: a new **ligand** of the **opiate** receptor.
AU Schiller P W; Lipton A; Horrobin D F; Bodanszky M
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, **(1978 Dec 29)** 85 (4) 1332-8.
Journal code: 9Y8. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 7906
CT Check Tags: Animal; Male; Support, U.S. Gov't, P.H.S.
Binding, Competitive
Biological Assay
Brain: ME, metabolism
*Cholecystokinin: ME, metabolism
Cholecystokinin: PD, pharmacology
*Endorphins
Endorphins: ME, metabolism
*Enkephalins
Enkephalins: ME, metabolism
Guinea Pigs
Ileum: DE, drug effects
Kinetics
Ligands
Peptide Fragments: ME, metabolism
Rats
***Receptors, Opioid: ME, metabolism**
Structure-Activity Relationship

L17 ANSWER 66 OF 70 MEDLINE
AN 78064347 MEDLINE
TI **Opioid** antagonists, endogenous **ligands** and nociception.
AU Jacob J J; Ramabadran K
SO EUROPEAN JOURNAL OF PHARMACOLOGY, **(1977 Dec 15)** 46 (4) 393-4.
Journal code: EN6. ISSN: 0014-2999.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 7804
CT Check Tags: Animal

***Ligands**
Mice
Morphine: AI, antagonists & inhibitors
Motor Activity: DE, drug effects
*Narcotic Antagonists: PD, pharmacology
*Pain: PP, physiopathology
Reaction Time: DE, drug effects
Receptors, Opioid: ME, metabolism

L17 ANSWER 67 OF 70 MEDLINE
AN 77219555 MEDLINE
TI Opiate receptor-natural ligand system: causal factor or defense system? [letter].
AU Torda C
SO AMERICAN JOURNAL OF PSYCHIATRY, (1977 Aug) 134 (8) 935.
Journal code: 3VG. ISSN: 0002-953X.
CY United States
DT Letter
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 7710
CT Check Tags: Animal; Human
*Animals, Newborn
Enkephalins: PH, physiology
***Ligands**
Mental Disorders: ET, etiology
Mental Disorders: PC, prevention & control
Models, Biological
Rats
***Receptors, Opioid**
*Stress, Psychological

L17 ANSWER 68 OF 70 MEDLINE
AN 77171375 MEDLINE
TI Endogenous **ligands** of **opiate** receptors.
AU Teschemacher H
SO NAUNYN-SCHMIEDEBERGS ARCHIVES OF PHARMACOLOGY, **(1977 Mar 31)** 297 Suppl 1 S51-2.
Journal code: NTQ. ISSN: 0028-1298.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 7708
AB From brain and from pituitary tissue of vertebrates several peptides - with molecular weights between 500 and 3500 daltons - have been isolated, which behave like opiates in opiate receptor binding assays, in isolated tissue preparations and in the intact animal.
CT Check Tags: Animal
*Brain Chemistry

Ligands
Oligopeptides
*Peptides: AN, analysis
Pituitary Gland: AN, analysis
***Receptors, Opioid: ME, metabolism**

L17 ANSWER 69 OF 70 MEDLINE
AN 77081070 MEDLINE
TI Endogenous opiate receptor ligand: electrically induced release in the guinea pig ileum.
AU Puig M M; Gascon P; Craviso G L; Musacchio J M
SO SCIENCE, (1977 Jan 28) 195 (4276) 419-20.
Journal code: UJ7. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 7704
AB Opiate receptors mediate the electrically evoked inhibition of the myenteric plexus-longitudinal muscle preparation of the guinea pig ileum. The electrically induced activation of the opiate receptor was produced by a prolonged simulation at 10 hertz and provides the first evidence that an endogenous opiate receptor ligand is released by nerve stimulation. The specificity of the phenomenon was demonstrated by the reversal obtained with the narcotic antagonists naloxone, naltrexone, and GPA 1843; GPA 1847, the (+)-isomer of 1843, did not cause reversal. The model system described should be useful for the study of the storage, synthesis, and release of endorphins.
CT Check Tags: Support, U.S. Gov't, Non-P.H.S.
Electric Stimulation
Ileum: IR, innervation
***Ligands**
Morphine: PD, pharmacology
Muscle Contraction: DE, drug effects
*Muscle, Smooth: IR, innervation
Naloxone: PD, pharmacology
Naltrexone: PD, pharmacology
Nerve Tissue Proteins: ME, metabolism
*Neuromuscular Junction: PH, physiology
Peptides: ME, metabolism
***Receptors, Opioid**
Receptors, Opioid: DE, drug effects
Stereoisomerism

L17 ANSWER 70 OF 70 MEDLINE
AN 77045174 MEDLINE
TI Enkephalin and drug dependence.
AU Hughes J
SO BRITISH JOURNAL OF ADDICTION TO ALCOHOL AND OTHER DRUGS, (1976 Sep)

71 (3) 199-209.
Journal code: AU8. ISSN: 0007-0890.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
EM 7703
CT Check Tags: Animal; Human; Support, U.S. Gov't, Non-P.H.S.
Chemistry
Heroin Dependence: ET, etiology
Leucine
***Ligands**
Lipotropin: PH, physiology
Methionine
Neural Inhibition
*Peptides: PH, physiology
Receptors, Opioid: DE, drug effects
***Receptors, Opioid: PH, physiology**
Substance Withdrawal Syndrome: ET, etiology